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2153-2236 2499-2621 2722-2856 3368-3523 4084-4227 4315-4423 4652-4777 5094-5193 5519-5647	HBGFS88	2628	914032	AC005369	10186	1-649
2499-2621 2722-2856 3368-3523 4084-4227 4315-4423 4652-4777 5094-5193 5519-5647						870-1459
2722-2856 3368-3523 4084-4227 4315-4423 4652-4777 5094-5193 5519-5647						2153-2236
3368-3523 4084-4227 4315-4423 4652-4777 5094-5193 5519-5647						2499-2621
4084-4227 4315-4423 4652-4777 5094-5193 5519-5647		ł		ļ.		2722-2856
4315-4423 4652-4777 5094-5193 5519-5647						3368-3523
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5094-5193 5519-5647						4315-4423
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		ł			11976-12107
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					14186-15261
HBGFS88	2628	914032	AC010687	10187	1-109
HBGFS88	2628	914032	AC005369	10188	1-109
HBGFS88	2628	914032	AC005369	10189	1-86
					357-503
HBGFG53	2629	727748	AC026666	10190	1-791
HBGFG53	2629	727748	AC026283	10191	1-1463
HBGFG53	2629	727748	AC026666	10192	1-244
HBGFG53	2629	727748	AC026283	10193	1-319
HBGFG53	2629	727748	AC026283	10194	1-297
					330-1653
HBGDA74	2632	832888	AP001100	10195	1-102
ļ					420-643
					761-840
ł		1		1	1681-1796
					1917-2066
					2158-2417
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					3281-3345
					3436-4001
					4062-4625
HBGDA74	2632	832888	AP000481	10196	1-64
					188-337
					429-688
		1			1350-1471
					1552-1616
					1707-2271
XXX CD 4 5 4	10.000	00000	1,500,00		2332-2895
HBGDA74	2632	832888	AP000481	10197	1-540
					1012-1076
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					1698-1760
	1				1787-1874
					1971-2103
					2575-2765
LIDCD A 74	2622	022000	A DO01100	10100	3027-3073
HBGDA74	2632	832888	AP001100	10198	1-540

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HBGBG52	2635	522424	AL136458	10199	1-294
1					506-707
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					5405-5870
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					7245-7361
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					9091-9694
					9825-10069
				1	10913-11066
				}	11815-12127
HBGBG52	2635	522424	AC069042	10200	1-245
HBGBG52	2635	522424	AL162739	10201	1-245
HBGBG52	2635	522424	AL136458	10202	1-112
HBGBG52	2635	522424	AL162739	10203	1-604
HBGBB78	2638	773930	AC008403	10204	1-1630
					2058-2480
}		1			4161-4577
					5334-5745
					6732-6865
}					7024-7163
		[			10746-11227
					12481-13862
HBGBB78	2638	773930	AC008403	10205	1-482
		1,,,,,,,	110000 105	10203	2074-2191
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					5313-5692
ŀ				}	10395-10491
					10694-10779
i					11107-11256
	Ì				12127-12209
			.		12283-12405
					12543-13031
HBGBB78	2638	773930	AC008403	10206	13771-14040
11000078	2030	113930	7000403	10200	172-232
					1302-2232
HBCPO75	2640	927520	AC069279	10207	1-596
			11000,21,		4098-4739
					5478-5650
L	<del>-1</del>			<del></del>	

				1	6045-6577
					6988-7374
HBCPK03	2641	922493	AC011719	10208	1-923
HBCPK03	2641	922493	AP001104	10209	1-923
HBCPK03	2641	922493	AP001324	10210	1-923
НВСЈР02	2642	917981	AP000795	10211	1-935
				1	1442-2055
					2120-2651
HBCJP02	2642	917981	AC018775	10212	1-935
				1	1442-2055
					2120-2653
HBCJP02	2642	917981	AC011088	10213	1-254
				1	1365-1474
					2669-2833
					3184-3483
					3853-4390 9055-9989
					10496-11109
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					15601-16949
					24077-24508
	1				25195-25367
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					28055-28776
					29078-30192
					35093-35409
					37099-37222
			į		37906-38308
					39047-39871
					40730-41079
					41464-41939
TID CIDOS	0640	017001	4.0011000	10014	42882-44161
HBCJP02	2642	917981	AC011088	10214	1-379
HBCJG07	2643	951898	AL158821	10215	1-179
IDCIC07	2643	951898	AL158821	10216	415-1143 1-401
HBCJG07	2043	931696	AL130021	10216	691-974
					1279-2180
HAUCC58	2644	764851	AC006329	10217	1-159
IACCCIO	2077	70-7051	AC000329	10217	388-562
					976-1372
					1647-1772
					1796-2110
	1		1		2230-2442
					3917-4291
					4695-4807

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					8183-8372
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		-			9645-9815
					10677-11353
				i.	11786-12287
	-				12400-13026
HAUCC58	2644	764851	AC006329	10218	1-338
					1214-1745
HAUAS89	2646	518847	AC008044	10219	1-119
,					2461-2803
					4346-4547
	J	ļ	}		5141-5577
					7669-7807
					7933-8244
				1	8849-8944
		1			9208-10426
					12618-12735
	1				13747-14129
				·	14744-15306
HAUAS89	2646	518847	AC008044	10220	1-55
					3400-3593
HAUAS89	2646	518847	AC008044	10221	1-495
HAUAQ28	2647	685374	AC027523	10222	1-1260
HAUAQ28	2647	685374	AC011774	10223	1-1260
HAUAQ28	2647	685374	AP001848	10224	1-1260
HAUAQ28	2647	685374	AC027523	10225	1-535
HAUAQ28	2647	685374	AC011774	10226	1-535
HAUAQ28	2647	685374	AP001848	10227	1-535
HACMR08	2650	955638	AC012318	10228	1-147
HACMR08	2650	955638	AL121844	10229	1-219
HACMR08	2650	955638	AC013553	10230	1-280
		}		1	2514-2880
					3507-3803
				}	5834-5958
					8010-8114
		1			9356-9430
				1	13100-13296
					14272-14676
					14966-15305
}					15968-16340
					16952-17049
					17302-17464
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					19824-20193
		1			20412-20822
	i				21304-21778
	1				22964-23210
					23327-23714
ļ	ļ			]	24031-24645
					24690-24771
L					26370-27118
HACMR08	2650	955638	AL121656	10231	1-2346
					2487-3703
					3832-4167

Table 1B summarizes additional polynucleotides encompassed by the [074] invention (including cDNA clones related to the sequences (Clone ID NO:Z), contig sequences (contig identifier (Contig ID:) contig nucleotide sequence identifiers (SEQ ID NO:X)), and genomic sequences (SEQ ID NO:B). The first column provides a unique clone identifier, "Clone ID NO:Z", for a cDNA clone related to each contig sequence. The second column provides the sequence identifier, "SEQ ID NO:X", for each contig sequence. The third column provides a unique contig identifier, "Contig ID:" for each contig sequence. The fourth column, provides a BAC identifier "BAC ID NO:A" for the BAC clone referenced in the corresponding row of the table. The fifth column provides the nucleotide sequence identifier, "SEQ ID NO:B" for a fragment of the BAC clone identified in column four of the corresponding row of the table. The sixth column, "Exon From-To", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO:B which delineate certain polynucleotides of the invention that are also exemplary members of polynucleotide sequences that encode polypeptides of the invention (e.g., polypeptides containing amino acid sequences encoded by the polynucleotide sequences delineated in column six, and fragments and variants thereof).

## TABLE 2

Clone ID	Contig	SEO	Analysis	PFam/NR Description	PEam/NR Accession	Cooro/	TIM	N.T.
NO.7	Ė	,	Mothod	Total Transcription	A T WILLIAM TALE CASSION	Score?		
7.00		NO:X	nomeral		Number	Percent Identity	From	To
H7MDD72	847688	13	blastx.2	(AF034780)	gb AAC98919.1	%56	597	7
				lysosphingolipid receptor Edg5 [Homo saniens]				
H7MDD72	887805	2651	HMMER	PFAM: 7 transmembrane	PF00001	118	75	899
			1.8	receptor (rhodopsin			•	
HAOSH55	952380	14	blastx.2	(AF200357) pantothenate	gb AAF23952.1 AF2	78%	2	337
				kinase 1 beta [Mus	00357_1		!	
				musculus]				
HAQAK73	764671	15	blastx.2	galactosylceramide-like	pir JC5238 JC5238	%59	129	7
				protein, GCP - human				
HAQBJ71	839982	18	blastx.2	BasR [Escherichia coli]	dbj BAA03143.1	%16	127	2
00010000	,					51%	392	123
HBCJS08	92828	23	blastx.2	(AK002129) unnamed	dbj BAA92096.1	%99	188	346
				protein product [Homo				
200000	70000	Š	,	Sapiciis				
HBGBG42	9.557.6	30	blastx.2	(AF161472) HSPC123	gb AAF29087.1 AF1	%05	85	315
מהשתיתו	030303			LIUMO Sapiens	014/2 1			
HBGB1/9	255525	33	blastx.2	Invasin. [Escherichia coli]	dbj BAA15799.1	%85	35	331
						46%	m	500
	,					87%	199	246
HBGBW60	954916	34	blastx.2	paired-like homeodomain	gb AAB39864.1	100%	101	235
				protein PRX2 [Homo				
				sapiens				
HBGDE85	524875	37	blastx.2	core protein [Escherichia coli]	gb AAA24544.1	%06	1	126
							_	

		_	_	_	_	_	_	_			_			_													
211		129	100	311			207		372	27.0	7/5	168	121	367			75		100	c c	c C	183	3		327	292	254
167		257	141	445			4		209	673	202	299	165	2			188		200	160	109	10	•		452	339	292
4.57		%98	92%	%08			88%		59.5	130/	6,0,7	43%	40%	%16			%16		019/	01 /0	9/25	26%			71%	93%	%69
PF00096		emb CAA29453.1		dbj BAA91205.1			gb AAA79137.1		PF00067	mir/ITTO676/ITTO676	n contributor that			gb AAD40286.1	•		gb AAC76465.1		dhilb A 01205 11	1:02102100		gb[AAD09338.1]	- -		dbj BAA06901.1	•	
PFAM: Zinc finger, C2H2	type	rhaR (AA 1-312)	[Escherichia coli]	(AK000496) unnamed	protein product [Homo	sapiens]	Fos-related antigen	[Rattus norvegicus]	PFAM: Cytochrome P450	cytochrome P450 2B -		green monkey		(AF156271) RING finger	protein terf [Homo	sapiens]	(AE000420) putative	regulator [Escherichia	(AK000496) unnamed	protein product [Homo	sapiens]	(AF022821) putative	potassium channel DP4	[Mus musculus]	alpha 1C adrenergic	receptor isoform 2 [Homo	sapiens]
HMMER	1.8	blastx.2		blastx.2			blastx.2		HMMER 2.1.1	blastx 2				blastx.2			blastx.2		blastx 2			blastx.2			blastx.2		
38				39			41		45					47			49		50			51			58		
971696				974223			870189		947112					848219			912730		952212			887152			918513		
HBGDS13				HBGDT43			HBGMD05		HBGMZ39					HBGND09			HBGNM13		HBGN007			HBGNQ31			HBGPH02		

60 113	hla	hlastx 2	(AE000157) orf	obl A A C 73617 11	7022	717	76
3		Ulabia.4	יווי (יכוסטידיה)	golywy 1301 / 1	0///	01/	05
	_		hypothetical protein		47%	555	346
		•	[Escherichia coli]		%91	619.	545
9		blastx.2	(AL137718) hypothetical	emb CAB70890.1	30%	21	581
7.0	12	Lloots 2	himmen classical factors	1. 7. 2021 C 1	7000	0,0	3
		lasta.2	1-delta [Homo sapiens]	emo CAA/9/10.1	13%	. 203	400
908	12	blastx.2	(AC008372) unknown	gb AAF23326.1 AC0	44%	-	270
			[Homo sapiens]	08372_2			
82 F	I 1	HIMIMER 1.8	PFAM: Zinc finger, CCHC class	PF00098	6.1	95	112
88 b	٩	blastx.2	unidentified reading frame	emb[CAA23893.1]	85%	211	152
			[Escherichia coli]		81%	311	264
					100%	264	226
					87%	325	302
92   bl	Ā	blastx.2	unidentified reading frame [Escherichia coli]	emb CAA23893.1	%86	334	158
94 bl	P	blastx.2	(AF141920) roadblock	gb AAD45986.1 AF1	75%	174	455
			[Drosophila melanogaster]	41920_1			
95 b	<u>.</u>	blastx.2	(AK000385) unnamed	dbj BAA91131.1	64%	499	335
			protein product [Homo		75%	266	195
			sapiens]		28%	336	286
96 P	<u> </u>	blastx.2	cytochrome P450 2C34v2	gb AAA79105.1	23%	94	189
	_		[Sus scrofa]		33%	9	98
98 86	9	blastx.2	(AK001623) unnamed	dbj BAA91793.1	.%68	183	440
			protein product [Homo				
	_		sapiens]				
105	<del></del>	HMMER	PFAM: Src homology	PF00018	5.22	179	214
		1.8	domain 3				

589				176		221			270	ì	258	170	252	23	}		210		216	21.0	3/18	276	2,4	453	283	305
182				114		18	}		178	•	169	06	169	76	•		371		300	202	28	-	1	370	179	234
100%				20.88		%6L			100%		100%	100%	%99	87%	•		72%		0 92		37%	28%		- %96	31%	9.4
emb CAA18266.1	-			PF00096		gb AAD37115.1 AF1	17814_1		emb CAB70754.1		gb[AAF08343.1]AF0	80470 1		gb AAB31222.1			dbj BAA91131.1		PF00023		gb AAB01605.1	emb CAA52297.11	-			PF00047
(AL022238) dJ1042K10.2	(supported by GENSCAN, FGENES and	GENEWISE) [Homo	sapiens	PFAM: Zinc finger, C2H2	type	(AF117814) odd-skipped	related 1 protein [Mus	[musculus]	(AL137469) hypothetical	protein [Homo sapiens]	(AF080470) pallid [Homo	sapiens]		truncated protein	[Saccharomyces	cerevisiae]	(AK000385) unnamed	protein product [Homo sapiens]	PFAM: Ank repeat	•	ankyrin 3 [Mus musculus]	putative [Rattus	nomyeoricinel	[cmarga tar		PFAM: IG (immunoglobulin)
blastx.2				HMIMER	1.8	blastx.2			blastx.2		blastx.2			blastx.2			blastx.2		HMMER	2.1.1	blastx.2	blastx.2			200	HMMER 1.8
									124		125			126			133		137			140			57.	142
			0,000	963100	<del></del>				851219		785121			887321			851213		823900			955291			70007	/8083/
			TITE A A A AO	HEAAA42					HEEAH07		HEEAJ58		, , , , , , , , , , , , , , , , , , , ,	HEEAJ/6			HEEAW01		HEGAB84			HEGAI82			TECA O92	ILEUA VOS

		superfamily				
149 HMMER 2.1.1		PFAM: Reprolysin family propeptide	PF01562	141.4	276	995
blastx.2		epididymal apical protein	emb CAA46929.1	%76	09	. 560
		I-precursor [Macaca fascicularis]				
151 blastx.2		ORF_D:0209#7	dbj BAA35540.1	83%	66	329
		[Escherichia coli]		81%	43	141
				%06	326	355
160 blastx.2		WW domain binding protein-1 [Homo sapiens]	gb[AAD10950.1]	100%	59	163
163 HMMER 1.8		PFAM: lipocalins	PF00061	26.73	117	509
blastx.2		(AF109472) epididymal	gb[AAC98311.1]	45%	314	99
		protein 52 [Oryctolagus cuniculus]				
169 blastx.2		(AK000385) unnamed	dbj BAA91131.1	23%	319	146
		protein product [Homo sapiens]				
179 blastx.2		(AJ243311) matrix	emb CAB46656.1	32%	262	636
	<u> </u>	metalloproteinase-2		39%	292	477
		[Equus caballus]		32%	24	569
1	-			27%	18	275
180 HMMER 1.8		PFAM: lipocalins	PF00061	11.52	208	627
blastx.14	<u> </u>	mE-RABP minor form	gi 3241966 gb AAC2	30%	502	630
		protein [Mus musculus]	4316.1	20%	336	482
1	$\dashv$			%09	279	308
2652   HMMER	_	PFAM: lipocalins	PF00061	11.52	405	524

			1.8					
			blastx.14	mE-RABP minor form	gi 3241966 gb AAC2	30%	399	527
				protein [Mus musculus]	4316.1	20%	233	379
						%09	176	205
HEQAE65	911438	181	HMMER	PFAM: Myosin head	PF00063	35.1	20	148
			2.1.1	(motor domain)				
			blastx.2	(AF234532) myosin X	gb AAF37875.1 AF2	100%	2	154
				[Homo sapiens]	34532_1			
HEQAH70	069669	182	blastx.2	(AJ007558) nucleoporin	emb CAA07553.1	%58	176	343
				155 [Homo sapiens]		%16	49	171
						%59	288	347
HEQAO76	769973	183	blastx.2	(AF053944) aortic	gb AAC25585.1	100%	148	201
				carboxypeptidase-like		100%	1	45
				protein ACLP [Homo		34%	592	430
				sapiens]		34%	269	400
						31%	329	433
						36%	311	424
						24%	792	415
		•		٠		21%	390	431
						35%	314	418
HETAF89	509300	189	blastx.2	(AF209069) hypothetical protein [Homo sapiens]	gb AAF16744.1 AF2 09069 2	%86	72	248
HETAH66	299662	191	blastx.2	IgE-binding factor [Mus	gb AAA37291.1	57%	109	216
				musculus]		37%	20	115
HETAZ13	536192	201	HIMIMER 1.8	PFAM: Src homology domain 3	PF00018	3.73	165	245
HETDI03	925489	217	blastx.2	zinc finger protein	gb AAC50260.1	78%	18	131
				ZNF133 [Homo sapiens]		%02	15	134
						74%	15	131

143	131	146	131	146	134	140	292		292	216	480		531		069		1146	434	262	347	294	392			440		
18	18	18	18	18	18	18	233		218	112	418		7		628	_	355	204	200	303	268	213			132		
%99	73%	%09	71%	62%	64%	%59	69.6		92%	61%	3.03		94%		9.64		72%	70%	%08	23%	%88	15.57			36%		
							PF00097		gb AAC40075.1		PF00293		emb CAA22894.1		PF00435		gb AAB01786.1		dbj BAA92096.1			PF00047			sp Q61581 Q61581		
							PFAM: Zinc finger,	C3HC4 type (RING finger)	(AF034745) LNXp80	[Mus musculus]	PFAM: Bacterial mutT	protein	(AL035291) hypothetical	protein [Homo sapiens]	PFAM: Spectrin alpha	chain, repeated domain	myosin II heavy chain	[Naegleria fowleri]	(AK002129) unnamed	protein product [Homo	sapiens]	PFAM: IG	(immunoglobulin)	superfamily	FOLLISTATIN-LIKE 2	(FOLLISTATIN-LIKE	FROIEIN).
							HIMIMER	1.8	blastx.2		HMMER	1.8	blastx.2		HMMER	1.8	blastx.2		blastx.2			HMMER	1.8		blastx.2		
							220				227				230				233			237					
							525407				799658				954104				973702			947978					
		<u>.</u>					HETDP21				HETFC82		-		HETFI24				HETFM43			HETGL74					

нетно63	745503	244	blastx.2	rhophilin [Mus musculus]	gb AAC52388.1	51% 35%	160	450
HETHR24	851412	246	HMMER 2.1.1	PFAM: Fibrillar collagen C-terminal domain	PF01410	53.4	201	308
			blastx.2	type V collagen [Gallus	gb AAB41274.1	<b>%59</b>	213	308
				gallus]	•	48%	98	214
						41%	336	437
HETIF01	966185	248	blastx.2	fused-ccdB [Escherichia coli]	emb CAA71575.1	94%	122	223
HETIJ84	766589	250	blastx.2	(AF161432) HSPC314 [Homo sapiens]	gb AAF28992.1 AF1 61432 1	75%	-	246
HETJX04	927120	262	HMMER 2.1.1	PFAM: C2 domain	PF00168	150.4	6	260
			blastx.2	(AB025258) granuphilin-a	dbj BAA84656.1	94%	9	683
				[Mus musculus]		21%	685	831
						48%	719	859
HETJY11	966194	263	blastx.2	(AK000496) unnamed	dbj BAA91205.1	%02	3	227
				protein product [Homo sapiens]				
HETKV26	910030	270	HMMER	PFAM: Oxysterol-binding	PF01237	19	2	364
חבתה שלכ	041045	07.0	L10-4- 14	A TOCACACAC	0014 4 1 1 00000011		(	3
HEINZON	941045	7/7	Dlastx.14	(Arue/9/2) DNA	gl4927370 gb AAD3	84%	63	200
				cytosine methyltransferase	3084.1[AF067972_1	72%	455	520
				3 alpha [Homo sapiens]		100%	520	537
HLWAH41	944774	283	HIMIMER	PFAM: ENV polyprotein	PF00429	150	82	714
			2.1.1	(coat polyprotein)			_	
			blastx.2	(AF108843) env protein	gb AAD34324.1	%05	19	711
				[Homo sapiens]				
HLWAI13	920690	284	blastx.14	(AL117538) hypothetical	g 5912069 emb CAB	100%	496	588

				protein [Homo sapiens]	55984.1			
HLWAJ64	746460	285	HMMER 1.8	PFAM: Zinc finger, CCHC class	PF00098	6.51	357	337
HLWAK69	694216	286	HMMER 1.8	PFAM: Zinc finger, C2H2 type	PF00096	6.05	118	168
HLWAR77	947484	288	HMMER	PFAM: 7 transmembrane	PF00001	214.2	1287	553
			1.8	receptor (rhodopsin family)				
			blastx.2	(AF119815) G-protein-	gb[AAD22047.1]	%66	1287	292
-		<u></u>		coupled receptor [Homo sapiens]				
HLWBQ84	782938	299	HMMER	PFAM: HMG (high	PF00505	9.46	21	110
			1.8	mobility group) box				
HLWFG82	929647	317	HMMER	PFAM: Immunoglobulin	PF00047	32.6	121	330
			2.1.1	domain				-
			blastx.2	Frazzled [Drosophila	gb AAC47314.1	37%	52	411
				melanogaster]		43%	488	535
HNOAX12	869363	330	blastx.2	line-1 reverse	gb[AAC51337.1]	41%	710	465
				transcriptase [Homo				
				sapiens				
HODAG37	529410	339	blastx.2	(AC004416)	gb AAC06181.1	24%	229	131
				WUGSC:H_RG013N12.g		28%	137	87
				w.1335199.a gene product				
				[Homo sapiens]				,
HODBT58	678444	355	blastx.2	(AF118086) PRO1992	gb AAF22030.1 AF1	%69		129
				[Homo sapiens]	18094 25			
HODCV09	973487	375	blastx.2	(AF034209) RIG-like 5-6	gb AAB92665.1	100%	130	207
				[Homo sapiens]				
НОДДОСТ	919295	392	blastx.2	(AF161393) HSPC275	gb AAF28953.1 AF1	%96	3	245

		67		225	707	±67			54			254	454		213			222		118		247		284		271	
		14		163	-	<b>-</b>			22			466	537		175			130		17		8		132		209	
	1000	100%	,	11.06	7052	0/75			9.2			48%	%09		3.15			6.61		94%		51%		%02	_	18.49	
71303 1	01393 I	1:06/1600	700000	PF00096	94 AAD19818 11	20 00000000000			PF00271			dbj BAA91205.1			PF00130			PF00102		sp Q9Y6Y5 Q9Y6Y5		sp Q9Y6Y5 Q9Y6Y5		gi 1196424 gb AAA8	8026.1	PF00096	
[Home conjunt]	(AV00161A) unnomed	protein product [Homo	sapiens]	PFAM: Zinc finger, C2H2 type	(AC007059) Himan	homolog of Mus musculus	wizL protein [AA 4-1561]	[Homo sapiens]	PFAM: Helicases	conserved C-terminal	domain	(AK000496) unnamed	protein product [Homo	sapiens]	PFAM: Phorbol esters /	diacylglycerol binding	domain	PFAM: Protein-tyrosine	phosphatase	IDN4-GGTR14	PROTEIN.	IDN4-GGTR14	PROTEIN.	pol gene protein; Xxx	[Homo sapiens]	PFAM: Zinc finger, C2H2	type
	blacty 2	7:37	40.61	HMMEK 1.8	blastx 2	7:57			HMMER	1.8		blastx.2			HIMIMER	1.8		HIMIMER	1.8	blastx.2		blastx.2		blastx.14		HIMMER	7.x
	307	<u> </u>		419					.423			451			459			463		465		466		471		477	
	567107		7007	189061					926260			934304			958329	•		973449		917969		926255		974297		908650	
	HODDS67		TOURDO!	HODERSI					HODEX10			НОБРО06			HODFY16			HODGC61		HODGH02		HODGH04		HODGJ67		HODGP95	

310	310	292	310	334	307	310	310	357	357	357	357	357	357	2	231		124	399	133	180	127	100	330		399	397	91
125	146	146	125	74	146	164	164	307	307	307	310	307	307	235	287		2	142	2	263	192	120	286	-	49	236	4
61%	25%	23%	41%	34%	20%	21%	46%	47%	47%	47%	20%	35%	41%	47%	21%		30.1	63%	72%	39%	45%	85%	1.62		72%	61%	20%
gb[AAC32422.1]	-				-									pir S72489 S72489			PF00620	gb AAB81198.1		gi 2318003 gb AAB6	6461.1		PF00052		gb[AAA60282.1]		
(AC005498) R31665_1	[Homo sapiens]	•												hypothetical protein	Tigger 2 - human	transposon MER37 1	PFAM: RhoGAP domain	(AC002398) F25965_3	[Homo sapiens]	unknown [murine	herpesvirus 68]		PFAM: Laminin B	(Domain IV)	ribosomal protein L7a	large subunit [Homo	sapiens]
blastx.2														blastx.2			HMMER 2.1.1	blastx.2		blastx.14			HMMER	1.8	blastx.2		
														479			481			207			512				
														974290			894368			932211			572941				
														HODGQ22			норедоя			HOFAD05			HOFMB78				

116	116	116	116	116	116	116	116	116	116	116	116	116	116	116	116	116	116	116	115	116	116	116	116	116	116	116	116	116	116
298	298	295	295	298	295	289	298	295	295	298	289	295	295	298	295	295	295	295	297	295	295	295	295	289	289	295	289	289	295
54%	46%	20%	21%	24%	80\$	51%	85%	48%	46%	25%	48%	43%	21%	46%	45%	43%	46%	45%	24%	43%	43%	45%	46%	44%	44%	43%	44%	46%	43%
emb CAA58337.1																		-											
U88 [Human herpesvirus	[9]																												
blastx.2																													
516																								·					
924679												•		•															
HOFMF03			-																										

						43%	295	116
						48%	289	116
						43%	289	116
						41%	295	116
					-,,	44%	342	115
						41%	339	115
						42%	297	115
HOFMF70	734917	517	HMMER 2.1.1	PFAM: Connexin	PF00029	20.4	244	288
			blastx.2	(AJ004856) connexin31	emb CAA06165.1	85%	113	259
				[Homo sapiens]		%02	285	386
HOFMG21	973358	818	HMMER	PFAM: MAS20 protein	PF02064	33.6	105	248
	-N		2.1.1	import receptor				
			blastx.14	mitochondrial outer	gi 285987 dbj BAA02	%86	114	416
				membrane protein 19	804.1	72%	452	484
				[Homo sapiens]			-	
HOFMH12	964722	519	blastx.2	19 kDa subunit of	emb CAA42218.1	%99	83	457
				NADH:ubiquinone		64%	312	476
				oxidoreductase complex				
				(complex I) [Bos taurus]				
HOFMH38	920365	520	HMMER	PFAM: TCP-1/cpn60	PF00118 ·	104.8	102	287
			2.1.1	chaperonin family				
			blastx.2	unnamed protein product	emb CAA02863.1	93%	09	296
				[unidentified]		%88	326	403
						100%	19	69
						100%	786	327
HOFMI62	796358	523	blastx.2	(AJ388527) Ribosomal	emb[CAB46829.1]	%96	40	228
				protein [Canis familiaris]		%96	231	323
						%99	320	355

						38%	35	88
HOFMJ44	719663	525	HIMMER 2.1.1	PFAM: Ribosomal protein S27	PF01667	109.1	128	265
		100	blastx.2	(AF070668) 40S	gb AAD20974.1	%56	99	274
				ribosomal protein S27				
				isoform [Homo sapiens]				
HOFMM72	464015	528	blastx.2	(AL117557) hypothetical	emb CAB55992.1	%59	19	366
				protein [Homo sapiens]				
HOFMP79	775242	531	HMMER 2.1.1	PFAM: GrpE	PF01025	46.4	173	358
			blastx.2	mt-GrpE#1 precursor	gb[AAC53534.1]	73%	173	400
				[Rattus norvegicus]		%98	36	164
HOFMQ65	789347	534	blastx.2	(AL050369) hypothetical	emb CAB43677.1	%89	113	343
				protein [Homo sapiens]		100%	43	147
						64%	354	404
HOFMS89.	575820	537	blastx.2	(AF161359) HSPC096	gb AAF28919.1 AF1	%29	181	411
				[Homo sapiens]	61359_1	46%	71	277
					-	%69	411	488
						72%	48	80
HOFMT43	811542	539	blastx.2	glucosephosphate	emb CAA82246.1	%05	. 143	514
				isomerase [Sus scrofa]		%08	57	161
						40%	277	501
HOFMT72	563575	541	blastx.2	Huntington Disease (HD)	emb CAA92991.1	82%	52	2
				gene exon 1 [Homo sapiens]		20%	297	256
HOFMU63	744325	543	blastx.2	(AK000334) unnamed	dbj BAA91091.1	63%	6	245
		·		protein product [Homo sapiens]				
HOFNA92	792734	547	blastx.2	(AL109701) C15orf3	emb CAB52022.1	%09	151	339

田	H)	Ħ	[Homo sapiens]		%98 %98	09	125
					37%	128	301
1	556	blastx.2	(AL133584) hypothetical	emb CAB63728.1	%06	80	241
			protein [Homo sapiens]		%06	99	95
					100%	253	270.
	558	blastx.2	(AJ224442)	emb CAA11944.1	81%	25	423
			methyltransferase [Homo sapiens]				
	561	HMMER	PFAM: Bacterial mutT	PF00293	4.34	286	345
		1.8	protein				
	562	HMMER	PFAM: Ribosomal L18ae	PF01775	250.8	62	331
		2.1.1	protein family				
		blastx.2	ribosomal protein L18a -	pir S03957 R5RT18	%£L	47	514
			rat				
	563	blastx.2	vimentin [Mus musculus]	dbj BAA19834.1	21%	204	377
					41%	175	396
-+					100%	140	178
	267	blastx.2	(AB026125) ART-4	dbj BAA86961.1	%65	146	451
			[Homo sapiens]		45%	18	479
	268	blastx.2	(AF086708) 26S	gb AAC64104.1	%46	46	204
			proteasome subunit 11		%56	200	259
-+			[Homo sapiens]		81%	261	308
	270	blastx.2	(AJ388527) Ribosomal	emb CAB46829.1	%96	85	273
			protein [Canis familiaris]		100%	276	362
					84%	365	403
-					38%	80	133
	572	blastx.2	(AF047704) tuftelin [Mus	gb AAC04577.1	%76	224	388
			musculus]		81%	127	222

143	425	477	369	233	43	347	388	179	73	257	504	790	643	989	40	151	293	377	431	377	82	500
69	393	427	13	87	23	141	347	78	2	216	205	650	599	200	177	20	225	93	111	132	2	81
%89	%06	28%	%08	%98	85%	43%	21%	47%	45%	45%	32.8	36%	%09	27%	%08	%02	68.7	%88	35%	34%	82%	32%
			gb AAD29427.1	gb AAA36383.1		emb CAB54316.1		gi 995826 gb AAC50	242.1		PF00077	gi 1397275 gb AAB0	3138.1		dbj BAA92096.1	gb AAF22025.1 AF1	PF00096	gb[AAB17949.1]				•
			(AF139185) myomegalin [Rattus norvegicus]	nucleobindin [Homo	sapiens]	T28D6.9 [Caenorhabditis	elegans]	cyclin A/CDK2-	associated p45 [Homo	sapiens]	PFAM: Retroviral aspartyl proteases	No definition line found	[Caenorhabditis elegans]		(AK002129) unnamed protein product [Homo	(AF118081) PRO1900	PFAM: Zinc finger, C2H2 type	Bowel [Drosophila	melanogaster]			
			blastx.2	blastx.2		blastx.2		blastx.14			HMMER 1.8	blastx.14			blastx.2	blastx.2	HMMER 2.1.1	blastx.2				
			579	580		582		584			591	592			602	909	615	-2.				
			751692	827631		606999		947431			890607	956896			706816	705406	909138					
			HOFOB88	HOFOB91		HOFOF57		HOGAF39			HOGCX95	HOGEE76			HOVBY34	ноусрз9	HOVEK70					

8 457	2 382	<u> </u>	3 108	7 234	7 326		<u></u>	5 10	8 148		3 232	1 384		461	569	604	3 238		355	205			40
368	212	92			237		279	96	89		89	304		384		449	89	,	149	00			249
33%	61%	53%	62%	82%	73%	35%	75%	75%	5.1		%96	%88	92%	23%	93%	78%	11.95		42	/0001	%/8	2	94%
	gi 3114713 gb AAC7 8826.1	gi 1196425 gb AAA8	8027.1	gi 531241 dbj BAA01	393.1			gi[2981631 dbj[BAA2 5253.1	PF00505		gi 4164442 gb AAD0	5419.1			emb CAB46721.1		PF00119		PF00047	951 05020 11AE1	11713 1		gi 5802182 gb AAD5
	(AF061346) Edp1 protein [Mus musculus]	envelope protein [Homo	sapiens	2-oxoglutarate	dehydrogenase precursor	[Homo sapiens]		(AB012223) ORF2 [Canis familiaris]	PFAM: HMG (high	mobility group) box	(AF044954)	NADH:ubiquinone	oxidoreductase PDSW	subunit [Homo sapiens]	(AL031427) dJ167A19.1	(novel protein) [Homo sapiens]	PFAM: ATP synthase A	chain	PFAM: Immunoglobulin	(AF111713) imetional	adhesion molecule [Homo	sapiens]	(AF159714) PPAR
	blastx.14	blastx.14		blastx.14				blastx.14	HMMER	1.8	blastx.14				blastx.2		HMMER	1.8	HIMIMER 2.1.1	blastx			blastx.14
	635	637		643				959	700		708				710		711		712				731
	922481	966158		967704				914115	960372		928614				925424		655753		884289				926787
	HPDOT03	HPDP169		HPDRG92				HPEKG18	HPFEA08		HPIAS40				HPIAX11		HPIAZ37		HPIBQ37				HPJCC04
												5	47										

				[Homo sapiens]				
HPJDA08	958182	741	blastx.14	zinc finger 5 protein [Gallus gallus]	gi 1399185 gb AAB3 8387.1	39%	92	475
HPJET90	836503	750	HIMIMER 2.1.1	PFAM: Aldehyde dehydrogenase family	PF00171	150.4	99	371
HPMEG50	925080	908	blastx.14	Mst84Dc [Drosophila	gi[11075 emb CAA47	62%	7	30
				melanogaster]	939.1	28%	22	105
HPMFL08	959569	819	HMMER	PFAM: Src homology	PF00018	44%	209	238
HPMGF06	954823	845	blastx.14	GTP binding protein [Mus	gi 53169 emb CAA36 803 11	92%	37	564
HPMGI03	924521	848	blastx.14	(AF106933) plexin B	gi 4056676 gb AAD0	36%	49	147
<del></del> -				[Drosophila melanogaster]	9426.1	%09	148	177
						63%	12	4
						43%	288	335
						%99	359	385
HPMGX23	575903	864	HMMER 1.8	PFAM: Helix-loop-helix DNA-binding domain	PF00010	99.9	96	194
HPMJF76	965642	875	blastx.14	pol protein [Human	gi 1780973 emb CAA	28%	234	326
				endogenous retrovirus K]	71417.1	40%	28	138
						63%	134	199
HPMJN59	946876	877	HMMER 1.8	PFAM: Prolyl oligopeptidase family	PF00326	21.87	138	251
			blastx.2	(AC005594) R26984_1 [Homo sapiens]	gb AAC33801.1	61%	138	521
HPMKM81	894416	884	HMMER	PFAM: Homeobox	PF00046	82.2	94	228
HPRCC08	939490	901	blastx.14	2.19 [Homo sapiens]	gj 854082 emb CAA6	54%	120	296

					0645.1			
HPWAS77	908450	914	HMMER   2.1.1	PFAM: gag gene protein p24 (core nucleocapsid protein)	PF00607	92.3	655	266
	_=		blastx.14	gag protein [Human	gi 1780975 emb CAA	37%	730	248
				endogenous retrovirus K]	71418.1	38%	185	108
						45%	253	188
						20%	25	2
HSWAC73	710354	926	HMMER 1.8	PFAM: WD domain, G- beta repeats	PF00400	66.6	134	190
HTEAL28	963538	939	blastx.14	(AL080154) hypothetical	gi 5262611 emb CAB	36%	234	413
	_			protein [Homo sapiens]	45745.1	?	3	
HTEBC74	887782	945	HIMMER	PFAM: Armadillo	PF00514	20.2	58	183
			1.8	segment protein, repeats			•	3
HTEBY08	960427	954	HMMER	PFAM: Protein	PF01240	92.8	63	251
	*		2.1.1	phosphatase 2A regulatory				
				subunit PR55				
	-		blastx.14	protein phosphatase 2A1	gi 619215 gb AAA58	%16	63	197
				B gamma subunit	956.1	87%	231	254
				[Oryctolagus cuniculus]				
HTECA21	911369	962	HIMIMER	PFAM: PDZ domain	PF00595	57.6	100	354
-			2.1.1	(Also known as DHR or				
				GLGF).				
			blastx.14	tyrosine phosphatase	gi 1486367 emb CAA	21%	85	351
				[Homo sapiens]	56124.1	51%	467	652
HTEDI02	921243	994	HIMIMER	PFAM: Leucine Rich	PF00560	36.2	346	414
			2.1.1	Repeat			2	•
			blastx.14	densin-180 [Rattus	gi 1657758 gb AAC5	36%	220	450
				norvegicus]	2881.1	32%	214	450

456	450	453	441	450	450	612	453	453	588	909	909	909	603	612	164	118	454	889	535	472	388	502	490	629	267	436	44
220	241	214	214	214	268	463	220	214	463	463	463	463	463	463	6	111	305	587	452	251	293	332	311	569	184	329	6
34%	30%	33%	78%	767	36%	36%	24%	792	40%	78%	762	31%	73%	24%	104.6	%99	46%	82%	21%	24%	78%	792	15%	24%	32%	25%	2.19
												,			PF00210	gi 5733824 gb AAD4	9751.1 AF176069_1										PF00099
															PFAM: Ferritins	(AF176069) ubiquilin	[Homo sapiens]										PFAM: Zinc-binding
															HMMER 2.1.1	blastx.14											HMMEK
															1007	1013										T	101/
															530589	932315										771505	(11202
										· <del>- · - · - · - · - · · · · · · · · · ·</del>				000	нтерозо	HTEDU48										UTED V20	nich is

			1.8	metalloprotease domain				
HTEDY54	922964	1018	blastx.14	lysozyme [Gallus gallus]	gi 63426 emb CAA43	46%	969	457
					319.1	41%	405	220
						%19	234	181
HTEGM38	675087	1059	HMMER   2.1.1	PFAM: DnaJ domain	PF00226	65.2	93	197
HTEGO05	932583	1061	HIMMER 2.1.1	PFAM: Eukaryotic protein kinase domain	PF00069	50.8	3	233
			blastx.14	male germ cell-associated	gi 205278 gb AAA41	85%	3	395
				kinase (mak) [Rattus	562.1	64%	489	761
	•			norvegicus]		82%	292	. 848
						38%	1023	1100
HTEHC47	973071	1085	blastx.2	unnamed protein product [unidentified]	emb CAB42447.1	79%	112	612
HTEHI14	526687	1096	HMMER	PFAM: lactate/malate	PF00056	50.6	222	371
			2.1.1	dehydrogenase				
HTEHS19	529280	11113	HMMER	PFAM: 7 transmembrane	PF00002	19.3	16	135
			2.1.1	receptor (Secretin family)	-			
HTEHV72	920610	11117	HIMIMER	PFAM: IQ calmodulin-	PF00612	41.7	178	240
			2.1.1	binding motif				-
HTEIB14	660896	1127	HIMMER 2.1.1	PFAM: Zinc finger, C2H2 type	PF00096	53.9	78	146
			blastx.14	Bowel [Drosophila	gi 1388166 gb AAB1	%06	6	236
				melanogaster]	7949.1	33%	6	230
						%08	227	316
						33%	6	230
						46%	6	149
						78%	54	230
						31%	230	334

316	381	380	426	275	792	707	400	406	406	406	406	406	406	137	406	409	431	431	431	431	431	263	216		225
224	307	297	358	117	188	25.7	333	353	353	353	353	368	356	09	353	326	411	411	411	408	414	192	1		1
35%	32%	32%	34%	64%	78%	7004	20%	20%	. 50%	%05	44%	%19	47%	45%	38%	44%	100%	85%	85%	81%	100%	11.27	34.7	-	70.1
				gi 4680715 gb AAD2 7747_1 AF132972_1	pil55471lemhlCAA38	020 11	1.076															PF00036	PF01490		PF00456 ·
				(AF132972) CGI-38 protein [Homo sapiens]	Zfo-29 [Mus musculus]																	PFAM: EF hand	PFAM: Transmembrane	amino acid transporter protein	PFAM: Transketolase
				blastx.14	blastx.14																	HMMER 1.8	HIMIMER	2.1.1	HMMER 2.1.1
				1128	1136																	1139	1148		1154
				958355	967431																	953803	941155		870652
				HTEIF40	HTEIK11						-						<u>.</u>					HTEIL07	HTEIP88		HTEIU92

HTEIV54	922027	1155	blastx.14	p18H-rev 107 [Rattus	gi 433963 emb CAA5	40%	359	682
				norvegicus]	3991.1	%59	251	364
HTEIY80	955242	1163	blastx.14	(AF146793) protein B	gi 4836805 gb AAD3	%16	320	454
				[Mus musculus]	0564.1 AF146793_1	74%	453	569
						83%	111	203
}						31%	257	322
HTEJE15	908360	1170	HMMER	PFAM: Helicases	PF00271	14.92	5	52
			1.8	conserved C-terminal				
				domain				
			blastx.14	vasa-like gene protein,	gi 806464 gb AAB33	73%	2	190
				RVLG protein=putative	364.1	84%	242	319
				DEAD 1 [Rattus sp.]		%59	188	265
HTEJF45	942476	1172	HIMIMER	PFAM: Zinc-binding	PF00099	2.28	593	637
			1.8	metalloprotease domain				
			blastx.2	(AB017800) nolp [Homo	dbj BAA34576.1	%69	135	299
				sapiens]		23%	290	487
						71%	523	549
						37%	540	629
HTEJP10	914785	1180	HMMER 1.8	PFAM: Heat shock hsp90 proteins	PF00183	13.29	110	214
HTEJP66	916481	1181	blastx.14	(AF151885) CGI-127	gi 4929723 gb AAD3	100%	499	639
	,			protein [Homo sapiens]	4122.1 AF151885_1	62%	979	706
HTEKS20	846714	1210	HMMER 2.1.1	PFAM: EF hand	PF00036	84.7	453	539
HTELE10	963563	1221	blastx.14	integumentary mucin B.1	gi 1184035 emb CAA	75%	339	244
				[Xenopus laevis]	64795.1			-
HTELJ89	966134	1229	HIMIMER	PFAM: Zinc-binding	PF00099	2.6	290	316
			1.8	metalloprotease domain				
HTELV86	910946	1252	HMMER	PFAM: Fibronectin type	PF00041	77.22	400	699

	918	1025	196	75	171	54	399	93	354	390	357	1054	225	1077	741	1161	849	1161	1360	927	1204	216	127	292	17	181	137
		096	926	22	_	-	786	10	280	274	286	1028	184	1057	658	247	253	955	1232	847	1169	302	171	348	55	231	100
	%96	%89	95%	%99	28%	25%	78%	42%	44%	33%	33%	100%	42%	100%	78%	320.7	42%	44%	22%	48%	28%	37%	23%	47%	23%	35%	7007
	gi 1016012 gb AAC5	2262.1														PF00022	gi 4204812 gb AAD1	1530.1				gj 4455041 gb AAD2	1045.1				
III domain	neural cell adhesion	protein BIG-2 precursor	[Rattus norvegicus]													PFAM: Actin	actin [Girardia tigrina]					(AF116463) unknown	[Streptomyces	lincolnensis]			
1.8	blastx.14															HMMER 2.1.1	blastx.14					blastx.14					
																1260						1273					
							,				-					911666						923066					
																HTEMA54						HTEMK03					

78	∞	629	103	286	286	286	292	286	304	286	286	286	286	283	286	283	866	931	280	383	226	319	337	450
134	43	12	35	2	2	2	2	2	2	2	2	2	5	2	5	7	606	998	20	240	80	122	143	331
42%	28%	%16	51.5	%19	26%	898	24%	25%	20%	23%	21%	21%	23%	21%	25%	21%	40%	45%	78%	37%	32%	62.3	47%	32%
		gi 5912114 emb CAB 55995.1	PF00096	emb[CAA55533.1															gi 2653671 gb AAC1	5893.1		PF00651	gi 3599513 gb AAC3	5368.1
		(AL117564) hypothetical protein [Homo sapiens]	PFAM: Zinc finger, C2H2 type	zinc finger protein [Homo	sapiens]														120 kDa style	glycoprotein [Nicotiana	alata]	PFAM: BTB/POZ domain	(AF086831)	leukemia/lymohoma related factor cLRF
		blastx.14	HMMER 2.1.1	blastx.2															blastx.14	,		HMMER 2.1.1	blastx.14	
		1280	1281																1284			1288		
		932319	909280																934338			913795		
		HTEMP49	HTEMR65										<del>-</del>						HTEMT06			HTEMX92		

				[Gallus gallus]				
HTENIS8	917213	1299	HIMIMER 2.1.1	PFAM: HMG (high mobility group) box	PF00505	118.2	308	514
			blastx.14	HMG-X protein [Xenopus	gi 639691 dbj BAA06	43%	269	514
				[aevis]	440.1	43%	101	319
						79%	88	214
						21%	446	487
HTENP54	787535	1306	HIMIMER	PFAM: Bacterial	PF00196	6.37	107	199
			1.8	regulatory proteins, luxR family				<u></u>
HTENP80	775387	1307	HMMER 1.8	PFAM: TPR Domain	PF00515	11.77	83	991
HTENR10	963530	1309	blastx.14	protein kinase related to	gi 1171248 gb AAC5	82%	10	132
				Raf protein kinases; 1	0354.1		1	
HTENR93	920834	1311	blastx.14	(AF121781) unknown	gi 4210989 gb AAD1	79%	285	644
				[Homo sapiens]	2066.1	74%	620	808
HIENY35	884043	1319	HMMER	PFAM: Zinc finger,	PF00097	95'9	449	592
			1.8	C3HC4 type (KING finger)				
HTEOF80	847224	1327	HMMER 1.8	PFAM: EGF-like domain	PF00008	14.65	20	100
HTE0136	870575	1330	HMMER 1.8	PFAM: HMG (high mobility group) box	PF00505	15.44	69	236
HTEON29	815852	1333	HMMER 1.8	PFAM: EF hand	PF00036	22.29	266	349
HTEOV90	870532	1336	HIMIMER	PFAM: Core histones	PF00125	11.37	358	435
HTEOW39	870566	1338	HIMMER	PFAM: C-type lysozymes	PF00062	126.92	59	295
			1.8	and alpha-lactabulmin				

482	575	442	442	488	2	180	201	211	158	689	590	435	411		669	171	195	141	447	78	65	177	645	340
225	483	2	2	408	}	4	<u> </u>	174	t 0	30	72	343	247		208	278	266	188	206	110	121	260	L	_
47%	%19	203	%89	51%		95.6	2	54%	42%	73%	21%	30.4	41%		36	30%	33%	43%	45%	54%	42%	25%	%05	28%
gi 2895085 gb AAC9	8478.1	PF00557	gi 2583129 gb AAB8	2638.1		PF00412		gil4205086lgblAAD1	0951.1	gi 4235350 gb AAD1	3183.1	PF00023	gi 747710 emb CAA3	4611.1	PF00035	gi 3638957 gb AAC3	6301.1		_				gi 4680715 gb AAD2	7747.1 AF132972 1
(AF004430) hD54+ins2	Isolorm Homo sapiens	PFAM: metallopeptidase family M24	(AC002387) putative	methionine	aminopeptidase [Arabidonsis thaliana]	PFAM: LIM domain	containing proteins	WW domain binding	protein-2 [Home sapiens]	(AF081947) tektin [Mus	musculus]	PFAM: Ank repeat	alt. ankyrin (variant 2.2)	[Homo sapiens]	PFAM: Double-stranded RNA binding motif	(AC004877) sco-spondin-	r to	P98167 l sapiens]						protein [Homo sapiens]
blastx.14	40,047	HMMEK 2.1.1	blastx.14			HIMMER	2.1.1	blastx.14		blastx.14		HMMER 2.1.1	blastx.14		HMMER 1.8	blastx.14						╅	olastx.14	
1340	1247	134/				1354		1356		1359		1366	•		1367	1371				_		1273	13/3	1
958391	022576	935370				870561		952243		947107		917406			840028	915198			-			1	730334	
HTEPA08	HTEPEOR	11111				HTEPM33		HTEPN07		HIEPP30		HIEPV02		Transfer	HIEPX32	нтеор40						HTEOE97	/0777111	

48	455		869		501	1096		898	1096	160	652	34	445	616	934	694	169	271	355	176	119		422
7	174		141		472	170		170	761	229	593	2	245	239	797	632	611	197	179	57	51		12
5.99	32.9		74%		3.53	345.2		%05	42%	23%	45%	63%	119.8	%19	78%	47%	40%	47.6	61%	42%	80.8		%01
PF00505	PF00335		gb AAF08363.1 AF1	33424_1	PF00293	PF00022		gi 290399 gb AAC80	574.1				PF00226	gi 3402485 dbj BAA3	2209.1			PF00096	gb AAA86728.1		PF00096		emb CAB36862.1
PFAM: HMG (high mobility group) box	PFAM: 4 transmembrane	segments integral membrane proteins	(AF133424) tetraspanin	TM4-B [Homo sapiens]	PFAM: Bacterial mutT	PFAM: Actin		actin 2 [Echinococcus	granulosus]				PFAM: DnaJ domain	(AB014888) MRJ [Homo	sapiens]			PFAM: Zinc finger, C2H2 type	Kruppel-like factor LKLF	[Mus musculus]	PFAM: Zinc finger, C2H2	type	(AL022067) dJ134E15.1
HMMER 1.8	HMMER	1.8	blastx.2		HIMMER	HMMER	2.1.1	blastx.14					HMMER 2.1.1	blastx.14				HMMER 2.1.1	blastx.2		HIMIMER	2.1.1	blastx.2
1379	1381				1383	1398							1402					1407			1409		
966141	939641				924799	911655							908832					908613			909254		
HTEQP45	HTEQR15				нтеот63	HTLCA95		,					HTLCY54					HTLDE64			HTLDF33		

				(Blimp-1) [Homo sapiens]		38%	24	392
HTLDG55	911645	1410	blastx.14	actin [Trypanosoma	gi 161963 gb AAA30	48%	95	199
				brucei	151.1	58%	28	63
HTLD094	915223	1413	blastx.14	(AC004667) hypothetical	gi 3668087 gb AAC6	37%	96	263
				protein [Arabidopsis	1819.1	34%	108	263
				thaliana]		37%	108	242
						44%	40	93
						30%	37	105
						38%	40	93
						29%	43	93
HTLDS55	891322	1416	HIMIMER	PFAM: Cell division	PF00735	454.7	233	1069
			2.1.1	protein				
			blastx.2	(AJ250723) septin-like	emb CAB59833.1	93%	131	1054
		·		protein Sint1 [Mus		<u>-</u>		
				musculus]				
HTLDT05	909752	1417	HMMER 2.1.1	PFAM: PH domain	PF00169	36.9	59	271
			blastx.2	(AK000004) FLJ00004	dbj BAA92229.1	77%	47	487
				protein [Homo sapiens]				
HTLDU05	911649	1419	HMMER 1.8	PFAM: Actins	PF00022	141.45	125	469
			blastx.14	(AF113908) actin-related	gi 4731565 gb AAD2	30%	2	469
				protein [Emericella nidulans]	8502.1 AF113908_1	33%	451	540
HTLEH30	934287	1429	blastx.14	(AF025310) tssk-1 and	gi 2739052 gb AAC0	%06	205	270
				tssk-2 kinase substrate	3366.1	28%	343	429
				[Mus musculus]		81%	306	338
HTLEJ11	973302	1431	HMMER 2.1.1	PFAM: Eukaryotic protein kinase domain	PF00069	55.9	44	223

blastx.14 (AF144573) Mx-interacting profein kinase	(4573) M3	K- ein kinase	gi 4868443 gb AAD3	69%	35	268
PKM		PKM [Mesocricetus	1-0.000	42%	293	397
auratus	===	ls]		38%	877	939
1444 HMMER PFAI	· >	PFAM: Actins	PF00022	262.03	134	703
blastx.14 actin	۳-	actin [Filobasidiella	gi 508701 gb AAC49	25%	143	715
ojoeu   neotc	$\equiv$	neoformans]	074.1	33%	787	963
				53%	721	804
1445 HWMER PFA	2	PFAM: Proprotein	PF01483	2169	38	433
2.1.1	อ	convertase P-domain				
1448 HMMER PFA	12	PFAM: Phorbol esters /	PF00130	1.97	172	225
1.8 diacylg domain	~ :=	diacylglycerol binding domain				
1451 blastx.14 (AC00		din-	gi 3638957 gb AAC3	%99	267	250
mucir P9816		mucin-like; similar to P98167 1 sapiens]	6301.1			
1459 blastx.14 (AJ0	0	(AJ007798) nuclear	gi 5834580 emb CAB	%98	12	731
protein sapiens]	.9 5	protein SA3 [Homo sapiens]	55312.1	%59	589	924
1462   blastx.2   (AF0	3	(AF053356) ORF4 [Homo	gb AAC78801.1	100%	77	256
sapiens	8	ns]		100%	3	77
				100%	376	420
1465 HMMER PFA	3	PFAM: Ubiquitin family	PF00240	83.86	42	324
1470 HMMER PFA	<del> </del>	PFAM: 'Cold-shock'	PF00313	70.2	3	158
k.14	اڅا	(AF096834) germ cell	gi 4837737 gb AAD3	%06	3	323

	specific Y-box binding   0662.1			393 485
pro	protein [Homo sapiens]			
				637 720
			63% 4	
blastx.14	a6(IV) collagen [Homo   gi 1850097 dbj BAA0	3AA0	48% 1	
	sapiens]   9791.1			
			61% 5	
				232 26
			37% 1	196 27
			66%	
HIMMER 2.1.1	PFAM: UBX domain PF00789		20.1 6	637 846
HIMIMER	PFAM: 'Cold-shock' PF00313		36.8	56 6′
				4
blastx.14	(AF096834) germ cell   gi 4837737 gb AAD3		%88	3   260
	specific Y-box binding   0662.1			330 44
	protein [Homo sapiens]			
				539 577
		-	34% 3	
			50%	572

613	634	479	140	531	363	479	284		243	358	455	270	308	475	749	542	46	137	137	137	137	187	240	293	187	281	387
584	209	342	54	460	256	402	195	_		287	402	235	240	152	591	465	7	3	8	8	45	128	181	234	128	234	340
%02	78%	23%	34%	37%	30%	30%	24.08		43%	%99	20%	28%	39%	83%	%09	%96	%99	37%	35%	33%	35%	45%	45%	45%	40%	20%	20%
							PF00076		gi 3925211 emb CAA	21539.1				gi 5230678 gb AAB6	2723.2			gi 482882 gb AAC46	499.1								
							PFAM: RNA recognition motif. (aka RRM, RBD,	or RNP domain)	(AL032626) cDNA EST	EMBL:D70654 comes	from this 1 1 1 yk377b8.3	comes f		(AF005038) secretory	carrier membrane protein	[Homo sapiens]		circumsporozoite protein	[Plasmodium vivax]								
							HMMER 1.8		blastx.14					blastx.14				blastx.14									
		•					1478		1481					1484				1486									
							933335		946586					936139				963475	•								
							HTLHP32		HTLHT15					HTLHV67				HTLHZ10									

					%04	181	240
					40%	128	187
					40%	128	187
•••					20%	287	334
					20%	287	334
					40%	234	293
					40%	128	187
					40%	181	240
					20%	234	281
					20%	340	387
				•	40%	287	346
					%05	128	175
					20%	258	293
		_			20%	202	240
					%09	311	346
945891	1488	blastx.2	(AC004410) fos39554_1	gb[AAC05601.1]	%49	9	275
			[Homo sapiens]		71%	292	417
					21%	257	319
942161	1495	HMMER 1.8	PFAM: Eukaryotic protein kinase domain	PF00069	251.19	166	933
		blastx.2	serine/threonine kinase	gb AAA99535.1	44%	133	936
			[Mus musculus]				;
953729	1496	blastx.2	(AF053356) ORF4 [Homo	gb[AAC78801.1]	%001	2	274
			sapiens]		100%	394	438
922923	1498	HMMER 1.8	PFAM: Src homology domain 3	PF00018	9.14	1152	1340
		blastx.2	(AL133030) hypothetical	emb CAB61362.1	94%	3	1355
·			protein [Homo sapiens]				
953714	1500	blastx.14	(AF025310) tssk-1 and	gi 2739052 gb AAC0	83%	m	206

715	391	548	464	542	334	20	813		813	405	124	1096	254		251		972	491	1049	96		129	129	237	129	237	129	234
554	263	516	468	510	260	21	445		448	37	813	980	18		93		466	105	861	22		1	-	-	-	-		13
74%	%56	72%	11%	63%	32%	%09	317.7		%58	%59	%08	19%	63.2		46.7		%68	<b>%96</b>	28%	42.8		%92	72%	45%	%19	44%	%19	%05
3366.1	•						PF01144		gi 164423 gb AAA31	019.1			PF01871		PF01769	,	dbj BAA91192.1			PF00096		emb CAA55529.1						
tssk-2 kinase substrate	[Mus musculus]						PFAM: Coenzyme A	transferase	succinyl-CoA:alpha-	ketoacid coenzyme A	transferase [Sus scrofa]		PFAM: Protein of	unknown function	PFAM: Divalent cation	transporter	(AK000480) unnamed	protein product [Homo	sapiens]	PFAM: Zinc finger, C2H2	type	zinc finger protein [Homo	sapiens]					
							HMMER	2.1.1	blastx.14				HIMIMER	2.1.1	HMMER	2.1.1	blastx.2			HMMER	2.1.1	blastx.2						
							1501		_				1515		1521					1532					-			
							924755			-			530564		973210					908937								
							HTLJJ75						HTTBJ94		HTTCT34					HTTD019								

190	287	190	190	287	287	221	227	190	649	352	827	424	1124			196		289	450	309			,	251	89	323	)	
125	180	149	191	180	180	180	180	26	536	197	759	377	195			47		8	292	73				102	9	282		
9%	36%	71%	%06	36%	36%	21%	20%	36%	25%	32%	25%	43%	84%			15.82		21%	26%	81%				44%	52%	6.83		
						•		gi 1098569 gb AAA8	2599.1		-		dbj BAA91592.1			PF00018		emb CAB41255.1		sp G545790 G545790				sp G545100 G545100	,	PF00175		
								glycosyl-phosphatidyl-	inositol-anchored protein	homolog [Mus musculus]			(AK001269) unnamed	protein product [Homo	sapiens	PFAM: Src homology	domain 3	(AL049683) hypothetical	protein [Homo sapiens]	DARPP-32=DOPAMINE	AND CAMP-	REGULATED	PHOSPHOPROTEIN.	SHB=SRC HOMOLOGY	2 PROTEIN.	PFAM: FAD/NAD-	binding domain in	oxidoreductases
	Ţ							blastx.14					blastx.2			HIMIMER	1.8	blastx.2		blastx.14				blastx.14		HIMIMER	1.8	
								1543					1556			1587				1594				1612		1639		
								618296					950051			911390				966804				928053		922064		
								HTTEU68					HTTFM66			HTTKP07				HUKAC72				HUVCQ07		HUVFH03		

110 253	_		295 366	147 335	135 362			395 159	151 110		2 391			216 278		201 314	101 169	134 355	_		185 403						
51.2		94%	87%	152.7	64%	55%		64%	75%		70.01	•		6.35		25%	39%	79.4		\ \ \ \	9//6	100%	100%	97% 100% 82% 100%	97% 100% 82% 100%	97% 100% 82% 100%	97% 100% 100% 98%
PF00651		gi 3287501 dbj BAA3	1223.1	PF01352	gil498152ldhilBAA06	541.1		dbj BAA91205.1			PF00201			PF00096		gi 3551182 dbj BAA3	2790.1	PF01423		pi 3289993 ph AAC2		5622.1	\$622.1  gi 4557143 gb AAD2	5622.1  gi 4557143 gb AAD2 2522.1 AF091457_1	5622.1  gi 4557143 gb AAD2 2522.1 AF091457_1	5622.1  gi 4557143 gb AAD2 2522.1 AF091457_1 dbj BAA06540.1	gi 4557143 gb AAD2 2522.1 AF091457_1 dbj BAA06540.1
PFAM: BTB/POZ domain		(AB011665) BAZF [Mus	musculus]	PFAM: KRAB box	ha0946 protein is	Homo	sapiens]	(AK000496) unnamed	protein product [Homo	sapiens]	PFAM: UDP-	glucoronosyl and UDP-	glucosyl transferases	PFAM: Zinc finger, C2H2	type	(AB012265) wizL [Mus	musculus]	PFAM: Sm protein		(AC005258) R30783_1		[Homo sapiens]	(AF091457) zinc finger	(AF091457) zinc finger protein RIN ZF [Rattus	[Homo sapiens] (AF091457) zinc finger protein RIN ZF [Rattus norvegicus]	[Homo sapiens] (AF091457) zinc finger protein RIN ZF [Rattus norvegicus] similar to human TRAMP	[Homo sapiens] (AF091457) zinc finger protein RIN ZF [Rattus norvegicus] similar to human TRAMP protein. [Homo sapiens]
HMIMER	2.1.1	blastx.14		HMMER 2.1.1	blastx.14			blastx.2			HMMER	1.8		HMMER	1.8	blastx.14		HIMIMER	2.1.1	blastx.14			blastx.14	blastx.14	blastx.14	blastx.14 blastx.2	blastx.14 blastx.2
1650				1653				1659			1668			1671				1673					1677	1677	1677	1677	1677
909169				908555				807696			933167			957834				957658				00000	930892	930892	930892	930892	930892
HUVGZ77				ноунс93				HVCAZ38			HVVBK72			HWLHJ68				HVVBY08					HUVGP05	HUVGP05	HUVGP05	HUVGP05 HUVF101	HUVGP05 HUVFI01

				receptor homolog 1	320.1 AF184971 1			
35	921132	1696	blastx.14	(AF151848) CGI-90 protein [Homo sapiens]	gi 4929649 gb AAD3 4085.1 AF151848 1	100%	2	94
95	957456	1710	HMMER 1.8	PFAM: Trypsin	PF00089	82.96	729	361
			blastx.2	(AF100707) testes-	gb AAF22500.1 AF1	100%	118	588
				specific protein TSP50 [Homo sapiens]	00707_1			
5	968333	1713	blastx.14	F35D2.4 gene product [Caenorhabditis elegans]	gi 861294 gb AAA68 328.1	47%	3	314
~	869612	1744	blastx.2	cDNA EST yk338f6.5	emb CAB04553.1	35%	587	345
				comes from this gene;	-	20%	999	589
				cDNA EST				
				EMBL:D75296 comes		-		
				from this gene				
,				[Caenorhabditis elegans]				
	926772	1748	blastx.14	(AF092091) cp431	gij3851160 gb AAC7 ·	45%	462	163
				[Rattus norvegicus]	2234.1	79%	195	118
	460948	1762	HMMER 2.1.1	PFAM: KRAB box	PF01352	79.1	282	401
ı	932997	1771	blastx.14	(AF036705) Similar to	gi 2749982 gb AAB9	%69	64	336
				phytoene desaturase;	5172.1	%89	373	468
- 1				coded for 1 1 coded for				
	946914	2997	blastx.14	acetylcholine receptor	gi 595481 gb AAA56	%9L	783	938
				alpha 9 subunit [Rattus rattus]	720.1	71%	586	720
10,	945862	1797	blastx.2	(AJ006692) ultra high	emb CAA07188.1	40%	21	272
				sulfer keratin [Homo	-	39%	21	272
				sapiens]				

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212	433	320	340	107	256	269	380	245	601	236	126	51	89	162	291		203		251	507	;	
108	380	186	302	9	203	213	294	156	239	186	9/	_	36	16	103		81	2	39	839		
34%	20%	792	23%	100%	100%	36%	26.93	12.29	%56	100%	%88	<b>%9</b> <i>L</i>	63%	37.78	92.6		7.86	2007	%99 %79	163.8		
gi 50489 emb CAA41	205.1			gi 5911890 emb CAB	55929.1		PF00036	PF00091	gi 2352998 gb AAB6	9345.1				PF00018	PF01772		PF01352	G 4 017-1075076515	81/3202300 emolCAB 45723.1	PF00387		
pro-alpha-2(I) collagen	[Mus musculus]			(AL117444) hypothetical	protein [Homo sapiens]		PFAM: EF hand	PFAM: Tubulin	(AF014461) EXO70	protein [Mus musculus]				PFAM: Src homology domain 3	PFAM: Isopentenyldiphosphate delta-	isomerase	PFAM: KRAB box	(AI 080125) himothetical	protein [Homo sapiens]	PFAM:	Phosphatidylinositol-	specific phospholipase C, Y domain
blastx.14				blastx.14			HIMMER 1.8	HMMER 1.8	blastx.14					HMMER 1.8	HIMMER 2.1.1		HIMIMER 2 1 1	blacty 14	PT-Waster	HIMMER	2.1.1	
1799				1804			1806	1810	1811					1821	1830		1834			1838		
963458				932882			772363	778180	961353		·			751985	920507		908528			948475	-	
HTLGS10				HTLEQ92			HTLEN77	HTLDZ81	HTLDW27					HTLBH67	HTFBE02		HTEQN83			HTEPE35		

			blastx.2	1-phosphatidylinositol-	pir S14113 S14113	48%	1	750
				4,2-01spnospnate phosphodiesterase 1				
HTEOY82	948845	1839	blastx.14	(AJ010949) calcium	gi 4186073 emb CAA	%16	165	374
				channel alpha-2-delta-C subunit [Mus musculus]	09423.1			
HTEMV66	813038	1852	HMMER	PFAM: Eukaryotic protein	PF00069	27.8	154	315
			2.1.1	kınase domain				
HTEMU66	944419	1853	HIMMER	PFAM: Eukaryotic protein	PF00069	114.85	613	963
			1.8	kinase domain				
			blastx.2	MEK Kinase 3 [Mus	gb AAB03535.1	46%	604	948
				musculus]		73%	209	340
HTEMO58	964769	1855	blastx.14	casein kinase 1 gamma 1	gi 854733 gb AAC52	82%	395	195
				isoform [Rattus	200.1	%59	482	423
				norvegicus]		87%	424	401
						77%	214	188
HTEKH17	942526	1867	blastx.2	(AF016184) putative	gb AAC53331.1	%02	300	88
				pheromone receptor		23%	605	378
				[Rattus norvegicus]	•	25%	85	29
HTEGJ74	765901	1892	HMMER 2.1.1	PFAM: Tudor domain	PF00567	38.5	9	167
нтерн90	909165	1924	HMMER 2 1 1	PFAM: BTB/POZ domain	PF00651	38.1	195	308
			blastx.14	(AF097916) HIV-1	9113860089l9hlA AC7	45%	150	308
				inducer of short	2973.1	39%	348	416
				transcripts binding protein				
				[Homo sapiens]				
HTEDH42	615250	1926	HMMER 2.1.1	PFAM: ADP-ribosylation factor family	PF00025	156.4	42	353

HTEDF22	908406	1935	HIMIMER	PFAM: Zinc finger,	PF00098	20.37	250	297
			1.8	CCHC class				
			blastx.2	nucleic acid binding	gb AAA89198.1	46%	52	303
				protein [Mus sp.]			-	
HTECC09	628829	1952	HMMER	PFAM: Zinc finger,	PF00097	14.18	261	338
			1.8	C3HC4 type (RING				
				finger)				
			blastx.2	(AF151048) HSPC214	gb AAF36134.1 AF1	%58	111	332
				[Homo sapiens]	51048_1			
HPWTA06	936026	1982	blastx.14	Collagenase precursor	gi 1742347 dbj BAA1	100%	624	454
				(EC 3.4). [Escherichia	5068.1	100%	359	207
				coli]		100%	457	362
			•			%85	216	115
						%49	169	98
HPWSA52	727294	1983	HMMER 1.8	PFAM: Homeobox domain	PF00046	11.67	215	262
HPWAJ39	575271	1993	HMMER	PFAM: Phorbol esters /	PF00130	2.68	81	122
			1.8	diacylglycerol binding domain	***************************************			 
HPRAG45	939849	2672	HIMMER	PFAM: WD domain, G-	PF00400	21.65	135	212
			1.8	beta repeats				
HPMGR15	660374	2040	HMMER	PFAM: Phorbol esters /	PF00130	2.84	307	333
			1.8	diacylglycerol binding				_
				domain				
HPLAI10	202896	2074	blastx.14	AT motif-binding factor	gi 1345408 dbj BAA0	33%	443	496
				[Mus musculus]	5046.1			
HPJEV95	929723	2076	HMMER	PFAM: ATP synthase A	PF00119	20.61	169	393
			1.8	chain				
HPJDT03	922815	2083	HMMER	PFAM: WW/rsp5/WWP	PF00397	9.71	294	371

			1.8	domain containing proteins	,			
HPJDA25	951281	2087	blastx.2	(AF047690) ATP-binding cassette protein M-ABC1 [Homo sapiens]	gb[AAD15748.1]	73%	291	488
HPJDA25	951284	2676	blastx.14	(AF047690) ATP-binding cassette protein M-ABC1 [Homo sapiens]	gi 4321407 gb AAD1 5748.1	87%	219	76
HPIAQ70	973604	2130	HMMER 1.8	PFAM: Flagella basal body rod proteins	PF00460	41.51	206	298
			blastx.14	Flagellar hook-associated protein 1 (hap1). [Escherichia coli]	gi 1651528 dbj BAA3 5891.1	77%	322 194	498
HPCTD03	922149	2191	HMMER 2.1.1	PFAM: Pterin 4 alpha carbinolamine dehydratase	PF01329	143.1	9	305
			blastx.14	pterin-4a-carbinolamine dehydratase [Homo sapiens]	gj848985 gb AAA69 662.1	62%	18	311
HPCOV68	911075	2195	blastx.14	(AC004500) GDF-9 [Homo sapiens]	gi 2996640 gb AAC0 8450.1	64%	2	160
HPCA089	946913	2196	HMMER 1.8	PFAM: Serpins (serine protease inhibitors)	PF00079	53.12	94	309
			blastx.2	leupin [Homo sapiens]	emb CAA61420.1	39%	309	327
HOVEE20	909030	2207	HMMER 2.1.1	PFAM: KRAB box	PF01352	105.4	229	348
			blastx.14	zinc finger protein 30 [Mus musculus	gil456269 emb CAA8 2913.1	67% 33%	193 367	348

	208	577	251	157	265	127	115	153		905	179	152	176	235	235	68	354	360	192		269	153	201
	464	458	204	2	158	5	5	4		753	9	3	33	188	191	18	259	190	139		150	64	271
	2.22	82%	43%	94%	94%	29%	27%	100%		38.5	63%	%89	%95	20%	46%	34.2	21.1	71%	83%	-	100%	%06	100%
	PF00099	gi 3290198 gb AAC2	5672.1	gi 3851160 gb AAC7	2234.1			gi 2944187 gb AAC0 5245.1		PF00348	sp G299838 G299838					PF00648	PF01265	gi 1209635 gb AAB1	9007.1		gi[1504012 dbj BAA1	3205.1	
domesticus	PFAM: Zinc-binding metalloprotease domain	(AF072860) protein	activator of the 1	(AF092091) cp431	[Rattus norvegicus]			(AF011336) putative E1- E2 ATPase [Mus	musculus]	PFAM: Polyprenyl synthetases	ZINC FINGER [CLONE	ZNF78L1].				PFAM: Calpain family cysteine protease	PFAM: Cytochrome c/c1 heme lyase	holocytochrome c-type	synthetase [Homo	sapiens]	similar to Human zinc-	finger protein,	BR140(P1:IC2069)
	HIMMER 1.8	blastx.14		blastx.14				blastx.14		HMMER 2.1.1	blastx.14					HIMMER 2.1.1	HMMER 2.1.1	blastx.14			blastx.14		
	2211			2244				2246		2261	2276					2286	2288				2301		
	932544			925784				925783		859016	908904					815822	953436				964682		
	HOVCOS0			HOOKF04				HOOJN04		HONAD02	HOGAM56					HOFNW65	HOFNW07				HOFNII0		

				[Homo sapiens]		%99	293	319
HOFNC80	835718	2303	HMMER	PFAM: IG	PF00047	11.98	148	291
		•	1.8	(immunoglobulin)				
				superfamily				
			blastx	(AF111714) junctional	gb AAD42051.1 AF1	71%	28	303
				adhesion molecule [Bos	11714_1	94%	306	362
				taurus]		33%	306	359
HOFMT55	888552	2311	HIMIMER	PFAM: Caspase	PF00619	43	111	239
			2.1.1	recruitment domain	-			
HOFMS43	947973	2313	HMMER	PFAM: Sushi domain	PF00084	64	174	302
			2.1.1	(SCR repeat)				
			blastx.2	porcine membrane	dbj BAA20476.1	41%	12	317
				cofactor protein [Sus				
				scrota				
HOFMP09	943358	2315	HIMIMER	PFAM: Immunoglobulin	PF00047	27.5	34	144
			2.1.1	domain				
			blastx	B-CAM [Homo sapiens]	emb CAA56327.1	%9L	31	351
						46%	300	494
						82%	473	553
						33%	247	372
						46%	283	327
						43%	91	138
HOFMF82	693987	2317	HMMER 1.8	PFAM: Zinc finger, C2H2 type	PF00096	10.91	44	106
HOFMF82	694062	2688	HMMER	PFAM: Zinc finger, C2H2	PF00096	53.7	372	440
			2.1.1	type				
HOFMF82	909248	2689	HMMER	PFAM: Zinc finger, C2H2	PF00096	48.3	19	129
			2.1.1	type				
			blastx.14	zinc finger protein [Homo	gi 495568 gb AAC50	52%	19	429

		_		sapiens	264.1	20%	55	429
						20%	25	402
						44%	79	429
						28%	4	99
HOFAF25	942367	2320	blastx.2	(AF036696) contains	gb AAB88349.1	39%	289	696
				similarity to Brassica				
				oleracea non-green 1				
				(GB:U13632)				
				[Caenorhabditis elegans]		į		
HODFF88	974911	2341	HIMMER	PFAM: Eukaryotic protein	PF00069	101.43	86	370
			1.8	kinase domain				
			blastx.14	mixed-lineage protein	pir S32467 JU0229	74%	131	493
				kinase 1 - human		81%	763	921
						30%	751	915
HODFD73	909812	2343	HMMER	PFAM: GTPase-activator	PF00616	34	190	390
			2.1.1	protein for Ras-like				
				GTPase				
			blastx.14	(AB016962) synGAP-b1	gi 4417207 dbj BAA7	%86	4	480
				[Rattus norvegicus]	4972.1			
HODCZ64	745966	2357	blastx.2	elastin like protein	emb CAA59990.1	75%	3	98
				[Drosophila melanogaster]		42%	364	405
						42%	358	399
HODAK55	745532	2383	HIMMER	PFAM: ATPases	PF00004	69.09	11	157
			1.8	associated with various				-
				cellular activities (AAA)				
HOCPH02	917453	2400	HIMMER	PFAM: Zinc finger,	PF00097	8.27	265	309
			1.8	C3HC4 type (RING				
				finger)				
HNIAB26	974750	2412	blastx.14	PR-1-like protein	gi 166861 gb AAA32	37%	388	143

$\dashv$
2419   blastx.14
2443 HMMER 1.8
2445 blastx.14
<del></del> .
2692 HMMER 1.8
2448 HMMER 1.8
HMMER 2.1.1
blastx.2
-
╅
2466 blastx.14
HIMMER 1.8
blastx.14
blastx.14

365	262	422	266	162	444	546	232	387		148	325	236	42	262	293	255	205	208	1,0	259	282	295	342
318	215	892	343	13	319	463	203	524		95	302	201	-	230	252	229	98	98	∞	206	94	260	178
93%	81%	73%	%69	24.44	38%	39%	40%	%16		44%	87%	20%	20%	45%	21%	%99	12.2	39%	39%	33%	82%	75%	59.48
		gi 4929709 gb AAD3	4115.1 AF151878_1	PF00141	gi 3116115 emb CAA	18866.1		gi 5231135 gb AAD4	1087.1 AF153605_1	gi 4760337 emb CAB	39078.2				gi 3873667 emb CAA	94874.1	PF00061	gi 56117 emb CAA42	493.1		gi 5225322 gb AAD4	0851.1[AF083108_1	PF00018
		(AF151878) CGI-120	protein [Homo sapiens]	PFAM: Peroxidases	(AL023286) hypothetical	protein	[Schizosaccharomyces pombe]	(AF153605) androgen	induced protein [Homo sapiens]	(AL034368) predicted	using hexExon; L779.3, 1				similar to collagen	[Caenorhabditis elegans]	PFAM: lipocalins	epididymal secretory	protein I (ESP I) [Rattus	norvegicus]	(AF083108) sirtuin type 3	[Homo sapiens]	PFAM: Src homology domain 3
		blastx.14		HMMER 1.8	blastx.14			blastx.14		blastx.14					blastx.14		HMMER 1.8	blastx.14			blastx.14		HMMER 1.8
		2488		2492	2500			2502		2513					2516		2525		_		2533		2554
		924849		827915	914044			941270		933091					922550		912065				930810		925952
		HEQCC01		HEQBG85	HEQAD73			HEPCB04		HEPAJ04					HEGBC03		HEEAX09				HEEAG51		HCOMIM05

HCHOX63 957690				D D D D D D D D D D D D D D D D D D D	46%	377	070
			rocentor kinges substrate		200	7 .	) i
			receptor kiliase substrate		43%	CII	435
			[Homo sapiens]		23%	43	222
-	90 2556	blastx.14	CDC42 GTPase-	gi 409027 gb AAA16	64%	112	597
			activating protein [Homo	142.1	78%	199	702
7			sapiens]				
HCHNW48   862478	78 2557	HMMER	PFAM: Laminin B	PF00052	1.52	230	289
7		1.8	(Domain IV)			:	
HCHMW18   966985	35 2559	blastx.14	(AB017614) OASIS	gi 4519621 dbj BAA7	100%	538	386
	· <u>-</u>		protein [Mus musculus]	5670.1	%89	440	222
1	$\dashv$				39%	308	240
HCHMI15   935298	98 2562	blastx.14	PSD-95/SAP90-associated	gi 1864093 gb AAB4	25%	181	582
		-)	protein-4 [Rattus	8590.1	15%	682	825
			norvegicus]		91%	584	169
1	1				20%	620	299
HCHAI62   743411	.1 2570	HMMER	PFAM: Core histones	PF00125	8.45	2	76
1		1.8	H2A, H2B, H3 and H4				_
HCDMC22   672815	.5 2578	HMMER	PFAM: Core histones	PF00125	9.49	182	241
$\exists$		1.8	H2A, H2B, H3 and H4				
HBGTT76   903653	3 2619	HMMER 2.1.1	PFAM: Ank repeat	PF00023	62.3	197	295
	·	blastx.14	(AJ133120) Proline rich	gi 5262748 emb CAB	72%	131	556
			synapse associated protein	45688.1	47%	499	561
7			2 [Rattus norvegicus]				
HBGMT82   954374	4 2624	blastx.14	(AJ004801) very large	gi 2653311 emb CAA	37%	187	267
	-		virion protein (tegument)	06097.1	35%	91	201
	_		Bovine herpesvirus type		32%	91	201
1	Ť		1.1				
HBGDF39 861602	72   2031	HMMEK	PFAM: Response	PF00072	44.82	158	355

			1.8	regulator receiver domain			
							L
HBCPV80	932817	2639	HMMER	HMMER   PFAM: WW domain	PF00397	64.2	 <u> </u>
			2.1.1				
HAOCD07	958959	2649	blastx.14	blastx.14 (AC005581) R31237_1,	gi[3510234 gb AAC3	100%	 108
,				partial CDS [Homo	3487.1		
				sapiens			

[075] Table 2 further characterizes certain encoded polypeptides of the invention, by providing the results of comparisons to protein and protein family databases. The first column provides a unique clone identifier, "Clone ID NO:", corresponding to a cDNA clone disclosed in Table 1A. The second column provides the unique contig indentifier, "Contig ID:" which allows correlation with the information in Table 1A. The third column provides the sequence identifier, "SEO ID NO:X", for the contig polynucleotide sequences. The fourth column provides the analysis method by which the homology/identity disclosed in the row was determined. The fifth column provides a description of PFam/NR hits having significant matches identified by each analysis. Column six provides the accession number of the PFam/NR hit disclosed in the fifth column. Column seven, "Score/Percent Identity", provides a quality score or the percent identity, of the hit disclosed in column five. Comparisons were made between polypeptides encoded by polynucleotides of the invention and a nonredundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFam"), as described below.

The NR database, which comprises the NBRF PIR database, the NCBI [076] GenPept database, and the SIB SwissProt and TrEMBL databases, was made nonredundant using the computer program nrdb2 (Warren Gish, Washington University in Saint Louis). Each of the polynucleotides shown in Table 1A, column 3 (e.g., SEO ID NO:X or the 'Query' sequence) was used to search against the NR database. The computer program BLASTX was used to compare a 6-frame translation of the Query sequence to the NR database (for information about the BLASTX algorithm please see Altshul et al., J. Mol. Biol. 215:403-410 (1990), and Gish et al., Nat. Genet. 3:266-272 (1993)). A description of the sequence that is most similar to the Query sequence (the highest scoring 'Subject') is shown in column five of Table 2 and the database accession number for that sequence is provided in column six. The highest scoring 'Subject' is reported in Table 2 if (a) the estimated probability that the match occurred by chance alone is less than 1.0e-07, and (b) the match was not to a known repetitive element. BLASTX returns alignments of short polypeptide segments of the Query and Subject sequences which share a high degree of similarity; these segments are known as High-Scoring Segment Pairs or HSPs. Table 2 reports the degree of similarity

between the Query and the Subject for each HSP as a percent identity in Column 7. The percent identity is determined by dividing the number of exact matches between the two aligned sequences in the HSP, dividing by the number of Query amino acids in the HSP and multiplying by 100. The polynucleotides of SEQ ID NO:X which encode the polypeptide sequence that generates an HSP are delineated by columns, 8 and 9 of Table 2.

[077] The PFam database, PFam version 5.2, (Sonnhammer et al., Nucl. Acids Res., 26:320-322, (1998)) consists of a series of multiple sequence alignments; one alignment for each protein family. Each multiple sequence alignment is converted into a probability model called a Hidden Markov Model, or HMM, that represents the position-specific variation among the sequences that make up the multiple sequence alignment (see, e.g., R. Durbin et al., Biological sequence analysis: probabilistic models of proteins and nucleic acids, Cambridge University Press, 1998 for the theory of HMMs). The program HMMER version 1.8 (Sean Eddy, Washington University in Saint Louis) was used to compare the predicted protein sequence for each Query sequence (SEQ ID NO:Y in Table 1A) to each of the HMMs derived from PFam version 5.2. A HMM derived from PFam version 5.2 was said to be a significant match to a polypeptide of the invention if the score returned by HMMER 1.8 was greater than 0.8 times the HMMER 1.8 score obtained with the most distantly related known member of that protein family. The description of the PFam family which shares a significant match with a polypeptide of the invention is listed in column 5 of Table 2, and the database accession number of the PFam hit is provided in column 6. Column 7 provides the score returned by HMMER version 1.8 for the alignment. Columns 8 and 9 delineate the polynucleotides of SEQ ID NO:X which encode the polypeptide sequence which shows a significant match to a PFam protein family.

[078] As mentioned, columns 8 and 9 in Table 2, "NT From" and "NT To", delineate the polynucleotides of "SEQ ID NO:X" that encode a polypeptide having a significant match to the PFam/NR database as disclosed in the fifth column of Table 2. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the polynucleotides of SEQ ID NO:X delineated in columns 8 and 9 of Table 2. Also provided are polynucleotides encoding such proteins, and the complementary strand thereto.

[079] The nucleotide sequence SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, the nucleotide sequences of SEQ ID NO:X are useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in Clone ID NO:Z. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to these polypeptides, or fragments thereof, and/or to the polypeptides encoded by the cDNA clones identified in, for example, Table 1A.

- [080] Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).
- [081] Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, and a predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing cDNA Clone ID NO:Z (deposited with the ATCC on October 5, 2000, and receiving ATCC designation numbers PTA 2574 and PTA 2575; deposited with the ATCC on January 5, 2001, having the depositor reference numbers TS-1, TS-2, AC-1, and AC-2; and/or as set forth, for example, in Table 1A, 6 and 7). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO:X.

[082] The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

## RACE Protocol For Recovery of Full-Length Genes

[083] Partial cDNA clones can be made full-length by utilizing the rapid amplification of cDNA ends (RACE) procedure described in Frohman, M.A., et al., Proc. Nat'l. Acad. Sci. USA, 85:8998-9002 (1988). A cDNA clone missing either the 5' or 3' end can be reconstructed to include the absent base pairs extending to the translational start or stop codon, respectively. In some cases, cDNAs are missing the start codon of translation. The following briefly describes a modification of this original 5' RACE procedure. Poly A+ or total RNA is reverse transcribed with Superscript II (Gibco/BRL) and an antisense or complementary primer specific to the cDNA sequence. The primer is removed from the reaction with a Microcon Concentrator (Amicon). The first-strand cDNA is then tailed with dATP and terminal deoxynucleotide transferase (Gibco/BRL). Thus, an anchor sequence is produced which is needed for PCR amplification. The second strand is synthesized from the dA-tail in PCR buffer, Taq DNA polymerase (Perkin-Elmer Cetus), an oligo-dT primer containing three adjacent restriction sites (XhoI, SalI and ClaI) at the 5' end and a primer containing just these restriction sites. This double-stranded cDNA is PCR amplified for 40 cycles with the same primers as well as a nested cDNA-specific antisense primer. The PCR products are size-separated on an ethidium bromideagarose gel and the region of gel containing cDNA products the predicted size of missing protein-coding DNA is removed. cDNA is purified from the agarose with the Magic PCR Prep kit (Promega), restriction digested with XhoI or SalI, and ligated to a plasmid such as pBluescript SKII (Stratagene) at XhoI and EcoRV sites. This DNA is transformed into bacteria and the plasmid clones sequenced to identify the correct protein-coding inserts. Correct 5' ends are confirmed by comparing this sequence with the putatively identified homologue and overlap with the partial cDNA clone. Similar

methods known in the art and/or commercial kits are used to amplify and recover 3' ends.

Several quality-controlled kits are commercially available for purchase. Similar reagents and methods to those above are supplied in kit form from Gibco/BRL for both 5' and 3' RACE for recovery of full length genes. A second kit is available from Clontech which is a modification of a related technique, SLIC (single-stranded ligation to single-stranded cDNA), developed by Dumas et al., Nucleic Acids Res., 19:5227-32 (1991). The major differences in procedure are that the RNA is alkaline hydrolyzed after reverse transcription and RNA ligase is used to join a restriction site-containing anchor primer to the first-strand cDNA. This obviates the necessity for the dA-tailing reaction which results in a polyT stretch that is difficult to sequence past.

[085] An alternative to generating 5' or 3' cDNA from RNA is to use cDNA library double-stranded DNA. An asymmetric PCR-amplified antisense cDNA strand is synthesized with an antisense cDNA-specific primer and a plasmid-anchored primer. These primers are removed and a symmetric PCR reaction is performed with a nested cDNA-specific antisense primer and the plasmid-anchored primer.

## RNA Ligase Protocol For Generating The 5' or 3' End Sequences To Obtain Full Length Genes

[086] Once a gene of interest is identified, several methods are available for the identification of the 5' or 3' portions of the gene which may not be present in the original cDNA plasmid. These methods include, but are not limited to, filter probing, clone enrichment using specific probes and protocols similar and identical to 5' and 3' RACE. While the full length gene may be present in the library and can be identified by probing, a useful method for generating the 5' or 3' end is to use the existing sequence information from the original cDNA to generate the missing information. A method similar to 5' RACE is available for generating the missing 5' end of a desired full-length gene. (This method was published by Fromont-Racine et al., Nucleic Acids Res., 21(7):1683-1684 (1993)). Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcript. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest, is

used to PCR amplify the 5' portion of the desired full length gene which may then be sequenced and used to generate the full length gene. This method starts with total RNA isolated from the desired source, poly A RNA may be used but is not a prerequisite for this procedure. The RNA preparation may then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase, if used, is then inactivated and the RNA is treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase. This modified RNA preparation can then be used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction can then be used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the reproductive system antigen of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the relevant reproductive system antigen.

[087] The present invention also relates to vectors or plasmids, which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC (deposited with the ATCC on October 5, 2000, and receiving ATCC designation numbers PTA 2574 and PTA 2575; deposited with the ATCC on January 5, 2001, having the depositor reference numbers TS-1, TS-2, AC-1, and AC-2; and/or as set forth, for example, in Table 1A, 6 and 7) is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as shown, for example, in Table 7. These deposits are referred to as "the deposits" herein. The tissues from which some of the clones were derived are listed in Table 7, and the vector in which the corresponding cDNA is contained is also indicated in Table 7. The deposited material includes cDNA clones corresponding to SEQ ID NO:X described, for example, in Table 1A (Clone ID NO:Z). A clone which is isolatable from the ATCC Deposits by use of a sequence listed as SEQ ID NO:X, may include the entire coding region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene. Furthermore,

although the sequence listing may in some instances list only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to sequence the DNA included in a clone contained in the ATCC Deposits by use of a sequence (or portion thereof) described in, for example Tables 1A or 2 by procedures hereinafter further described, and others apparent to those skilled in the art.

- [088] Also provided in Table 7 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.
- [089] Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128,256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into E. coli strain XL-1 Blue, also available from Stratagene.
- Obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus 15:59-* (1993). Vector lafmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR®2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).

[091] The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the deposited clone (Clone ID NO:Z). The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

- [092] Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of reproductive system associated genes corresponding to SEQ ID NO:X or the complement thereof, polypeptides encoded by SEQ ID NO:X or the complement thereof, and/or the cDNA contained in Clone ID NO:Z, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.
- [093] The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.
- [094] The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.
- [095] The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988).

Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the reproductive system polypeptides of the present invention in methods which are well known in the art.

The present invention provides a polynucleotide comprising, or alternatively [096] consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA sequence contained in Clone ID NO:Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X or a complement thereof, a polypeptide encoded by the cDNA contained in Clone ID NO:Z, and/or the polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X. a polypeptide encoded by the cDNA contained in Clone ID NO:Z and/or a polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO:X, a nucleic acid sequence encoding a polypeptide encoded by the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA contained in Clone ID NO:Z.

[097] Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in Table 1B column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in Table 1B column 6, or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides

of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[098] Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1) and have a nucleic acid sequence which is different

from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

Further, representative examples of polynucleotides of the invention comprise, [099] or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1B, column 2), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1B, column 2), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (See Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and

variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

Moreover, representative examples of polynucleotides of the invention [0100] comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of Table 1B column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in the same row of Table 1B column 6, or any combination thereof. In preferred embodiments, the polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in the same row of Table 1B column 6, wherein sequentially delineated sequences in the table (i.e. corresponding to those exons located closest to each other) are directly contiguous in a 5' to 3' orientation. In further embodiments, above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[0101] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B, and the

polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1B, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of SEQ ID NO:X correspond to the same Clone ID NO:Z. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[0103] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of SEQ ID NO:X correspond to the same row of column 6 of Table 1B. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[0104] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-

described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0105] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X are directly contiguous Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0106] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0107] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or

alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides, are also encompassed by the invention.

[0108] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0109] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 corresponding to the same Clone ID NO:Z (see Table 1B, column 1) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0110] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one sequence in column 6 corresponding to the same contig sequence identifer

SEQ ID NO:X (see Table 1B, column 2) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0111] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3'10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 corresponding to the same row are directly contiguous. In preferred embodiments, the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B is directly contiguous with the 5' 10 polynucleotides of the next sequential exon delineated in Table 1B, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the abovedescribed polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0112] Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. Accordingly, for each contig sequence (SEQ ID NO:X) listed in the third column of Table 1A, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO:X, b is an integer of 15 to the final nucleotide of SEQ ID NO:X, where both a and b correspond to the positions

of nucleotide residues shown in SEQ ID NO:X, and where b is greater than or equal to a + 14. More specifically, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a and b are integers as defined in columns 4 and 5, respectively, of Table 3. In specific embodiments, the polynucleotides of the invention do not consist of at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. as disclosed in column 6 of Table 3 (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence(s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone). In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example. All references available through these accessions are hereby incorporated by reference in their entirety.

## TABLE 3

	Accession #'s		AI139000, AA884996, AA889649, and AA724461.	AW182856, AI218191, AA834537, AA804628, AA827835, AF034780, and E07989.	AI681511, AA677498, AI799484, AI360937, AI378075, AI457270, AI363333, AI681227,	AI806180, AI363339, AA972313, AA627925, AI984311, AA483815, N25951, AI250808,	AI417147, AW297301, AI079688, AW009637, AI289263, AA768395, AA769533, AW085089,	AW368116, AW067835, AI110587, N26848, W15533, AI129095, AW298190, AI300955,	AI870137, AW410019, AI808400, AA748383, AA479673, AW269239, AA281561, AA807144,	AW291197, AW373450, and N42781.	H93040, H93056, AA719305, AA808945, AI342677, AA742815, AC006581, AP000045,	AP000113, AC007684, AC002404, AC003070, AC003042, AP000327, AC003043, AC005829,	AB023048, AP000123, AP000170, AP000055, AC007066, AC002350, AC005399, AL135744,	AC005031, AF001549, AC004913, Z95114, AL031663, AL008729, Z97054, AL133355,	AC000381, AC005207, AC009516, U80017, Z81370, AC006023, AC006449, AC005296,	AC005069, AC000118, AC004821, AC006146, AC005037, AC006441, AL109798, AL031432,	AL080243, AC004819, AL109627, AC002477, and AC004882.					AW168869, and AI904433.		AW419224, AW419225, and AW419223.	AL119483, AA809125, AL119444, AA835346, AA188940, AC016027, AC016830, AC005529.	AC005261, AC004531, AC005255, AC006137, AC006080, AL049874, AL132777, L44140,	AL031983, AC006515, AC004659, Z85987, AC005531, AF134726, AC006441, AC004858,	AF053356, AP000552, AC005740, AP000503, AC012627, AC004882, AC003108, AC007934,	AL049758, AC005181, AF109907, AC004033, AC005091, AC007685, AC005971, AC003663,	AC005274, AC005089, AL049829, AC006449, U96629, AC004973, AL049872, AC007283,	AC005057, AC004231, AL035413, AL078638, AC006023, AC005815, AL031311, AL023803,	AC005821, AL049780, AL031228, AC005919, AP000555, AL049631, AC004895, AC005072,	AC005/36, AL021155, AL022165, AL133448, AL133245, AC007055, AL008718, AC004526.
	claimer Range of b	15 - 73	15 - 162	15 - 606	15 - 708	-					15 - 742							15 - 361	15 - 70	15 - 423	15-97	15 - 724	15 - 135	15 - 338	15 - 506								
	EST Disclaimer Range of a Range	1 - 59	1 - 148	1 - 592	1 - 694	_					1 - 728							1 - 347	1 - 56	1 - 409	1 - 83	1 - 710	1 - 121	1 - 324	1 - 492								
	Contig ID:	928554	722780	847688	952380					+	764671							664979	783259	839982	522004	847519	529711	968339	928786								
SEQ	S S ×	11	12	13	14						15							9	17	18	16	20	21	22	23								
	Clone ID NO: Z	H7MCE35	H7MDC49	H7MDD72	HAOSHSS						HAQAK73							HAQAM17	HAQBF84	HAQBJ71	HAQBQ50	П			HBCJS08								

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					AL109758, Z70281, AC004859, AC005081, AL079295, AC002425, AB026898, AC004985,
					AL035072, AC005484, AC004816, AC005914, AL121754, AC004890, AC005746, AL121757, Z86090, AL109627, AL133163, AC000003, AC009721, Z82250, AC007057, and AC005071
HBCPD14	24	963634	1 - 127	15 - 141	
HBCQ103	25	922401	1 - 124	15 - 138	AW392670, Z99396, AL119319, AL036418, AL036858, AW372827, AW384394, AL119457,
					AL119483, AL119324, AW363220, AL119484, AL119391, AL119497, AL119522, U46351,
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					AL119496, AL119439, AL134536, AL036196, AL037082, AL119444, AL134525, AL036268,
				***	U46346, AL038837, AL042614, AL134920, AL043019, AL042984, AL037051, AL042965,
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					A81671, AB026436, AD001527, AR054110, AR023813, AR064707, and AR069079.
HBCQS90	76	951787	1 - 507	15 - 521	AA191298, AW364854, AI205727, R16601, and AI188004.
HBCQS93	27	930682	1 - 607	15 - 621	AA703200, W88470, and Z39990.
HBGBD28	28	525846	1 - 314	15 - 328	
HBGBF56	29	957870	1 - 240	15 - 254	
HBGBG42	30	922396	1 - 689	15 - 703	N33183, AA169202, AI393342, AW172574, AA731731, AI961101, AA872188, W17122,
					AI219418, AA609341, AA485152, AW293905, AI221103, AI910881, AW195626, AA856740,
					AA767183, AW072218, AA929018, AI338682, AA836394, AA448345, AW293908, AI264116,
					W26762, AA766127, AA761418, H30745, AA315954, AI022328, AI032738, AI203338,
					AI/68542, AI979322, AA470714, AA303837, AA992529, AA764904, AA627584, AA769119,
					AA169659, AI217749, W70324, AA333338, AI250852, AI635634, AI147877, AI382313,
					AL3 / /000, AL3 20946, AL955310, AL036241, AI638523, AI589668, AA814517, AA001397,
					AL096773, AF122922, and Y14314.
HBGBH43	31	524532	1 - 183	15 - 197	AI863446, AI188331, AW014913, AI073437, AW291378, AI130693, AI768987, and
HRGBS07	33	954799	1 - 403	15-417	A A A 200077 NAT 1981 N72545 TY70800 TEATAM A MYSSONIC 1 A A ESCACIO
HBGBT79	33	525352	1-318	15 - 332	12 12 12 13 13 13 13 13 13 13 13 13 15 15 15 15 15 15 15 15 15 15 15 15 15
HRGRW60	37	054016	1 555	15 560	A1000770 A1000700 A1000000 A1000000 A1000000 A100000000
NO W COCKET	5	224210	1 - 223	10 - 209	Alous 2/8, A109/30/, A19365/0, AW16/940, A13/9188, A1669686, A1751739, AW450137,

AI868311, AI203915, AW182104, AW014255, AI766481, AI821507, AA548667, AA194990, AF061970, U81600, and X52875.
15 - 507
15 - 139
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				Z84484, AL049776, Z98949, AC005295, AL078603, L29074, AL049853, AC005296, U67825, X55929, M22900, AC004076, AL050348, AL049736, AL022725, AB014079, AD0000833, AL121778, U29953, Z82245, Z69713, AF002993, Z92845, AL131494, AC005306, U76377
- 15				Z92846, AC006139, AC002384, AL022311, AF104455, AC007033, AP000339, AF157623, AP000326, AL008728, AC004389, AF038458, AF095725, AP000054, AP000169, AP000123,
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				AC005920, AC007297, AC006312, AC002316, AC004161, U95739, AL023575, Z95113,
				AL110502, AC006538, AP000517, AC007567, AL021977, D83989, U18390, X55932, AC003029 AL109799, AC005193, AC002119, AL00759, AL0259, AL02599, AC002119, AL00759, AL0259, AL0259, AL0259, AL02599, A
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				AF006752, AC004036, AC005620, AC002314, AF039907, AC002984, AC005175, AC004205,
				AC007,303, AC004211, AC007,223, AL043639, AF000401, AC003500, AC003,01, AC003619, AL080242, AP000261, AL031273, AC006388, AC006561, AC0065072, AF146367, AC002390,
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				297196, AC002559, AP000246, AL024474, AF190465, AL008710, AL031594, AL022240,
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<u>.</u>				AC006037, AC004226, AL050401, AC007242, AL04699, AC006339, AC006428, AC00533,
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				AC006019, AC004933, Z97056, AL034561, AC005244, AL078624, AF118808, AF207550,
+				AC007228, and AC004883.
HBGFA62   40	954306	1 - 628	15 - 642	AI479262, AW082836, AA877924, AA513292, AA700228, AI244885, AL041763, AI345227,
				AW2/3318, D25/18, AW001271, AI902419, AA687630, AI349742, AI306060, AI309420, AI307478, AI343141, AW075033, AI36766, AI371550, AI3075143
HBGMD05 41	870189	1 - 575	15 - 589	AW393804, AW001436, W42981, AI766185, AA706041, AI365102, AI380655, AW290901.
-				and AI126989.
-	933763	1 - 315	15 - 329	298258.
HBGMF10   43	966132	1 - 555	15 - 569	AA532449, AA043318, AI872402, AI524324, AA527086, AA514662, AA659799, AA971274,
				AA470758, AA602448, AI022054, AA861977, AI636322, AI865691, AI209021, AI055999,
				AA040380, AA033310, 132938, AI313402, AA038606, AW166625, AW004703, AI348693,

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AA436104, T61144, T52957, AI696664, AA043317, AW449638, AA129864, AI499456, AI972817, AI424348, AI918494, and AA436005.		A1820661, A1791493, AA989356, A1791282, A1732537, A1792053, AW207804, R22360, R72427, AA505927, R22019, and R72474		AA781868, AW152318, AA482996. AA909463, AA758672, and AF156771	AC004156.	AW177440, C14389, T03269, AI905856, AW352117, AW179328, AW360811, AW178893, AW366296, AW375405, D58283, AW378532, D59859, D80022, C14331, D80166, D80195, AW376501, D80193, D59927, D59467, D51423, D59619, AW177511, D80190, D51799, D80391, D80164, D59275, D80240, D80253, D80043, D59787, D80227, D59502, D81030, D80212, D80196, D80188, D80219, C14014, AW176467, C15076, D80038, D80269, D59610, D57483, D80196, D80188, D80219, C14014, AW176467, C15076, D80038, D80269, D59610, D57483, D80366, AA305409, C14429, D51022, D50979, D50995, D59889, AW178762, D51060, AW375406, AW377671; D80378, AW178775, AW360844, D80045, AW37671, AW375671, AW377671, AW377671, AW377671, AW377671, AW377671, AW377671, AW377671, AW377676, AW177731, AW178907, AW178906, D80248, AW179019, AW179024, D80522, AA514186, AA514188, C75259, D80133, AW177055, AW179020, D58253, AW178999, AW178911, D80439, D80132, AW178974, AW352174, T48593, AW177723, AW178911, D80439, D80132, AW17874, AW352174, T48593, AW177723, AW178983, D51103, AW367950, AR066482, I18367, A44171, A85477, I19525, A86792, I50126, I50132, I50128, I50128, A25909, AR066482, I18367, AR062274, Y09669, AR066490, AR016514, D13509, D50010, AR06138, A45456, A26615, AR068498, U79457, AR060133, AF135125, and AR0088278.	AA488707, AA129219, H49568, AI345366, AI310873, AA476397, AA535216, AA086368, AI268334, AI268336, AW021583, AI500453, AA420998, AA421078, AA657835, AL041345, T11634, AA601327, AA431949, AI762314, AA676971, AW157005, AA346367, AI537041, AW008450, AA600869, AA346368, AI051037, AA493621, AA57209, AA186329, AA533281, AA186367, AA579367, AA683238, AA18861, AI884383, AA744018, AA776899, N23392, AL038736, AA478716, N29455, AI702314, AW276835, AA833896, AA833875, AA484373, H56430, AI028510, AA992126, AA 579908, AW180384, H40091, AI464500, AA 57544
	15 - 342	15 - 602	15 - 237	15 - 1178	15 - 331	15 - 362	15 - 383
	1 - 328	1 - 588	1 - 223	1 - 1164	1 - 317	1 - 348	1 - 369
	845194	947112	958257	848219	914594	912730	952212
	44	45	46	47	48	64	50
	HBGMG29	HBGMZ39	HBGNA08	HBGND09	HBGNJ14	HBGNM13	HBGN007

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					AL390380, AL031710, AC007617, D32060, AC004859, AC008372, AL079340, U52112, AL022311, AC002364, Z74739, AC005089, AL023575, AL031779, AL033522, AL035086, AC011331, Z93783, Z82249, AL022237, AL049643, AD000684, AC007178, AL080242
			•		AC000056, AL022150, AL049538, AC005800, AL109657, AC002565, AL022312, AC007242, AP001054, AL031296, AL02498, AC002312, AC005189, AC004032, AF048779, AC007787
					AC004017, AC007999, AL022320, U78027, AC004548, AC005091, AC005833, AL035422,
				<del></del>	AC00022, AC00710, AC000013, AL121769, AL022163, AC004887, AC007055, AC009498, U47621, AC006166, AB023051, AC004099, AC005027, AP000512, AL031466, U89337,
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					Z98048, AC003688, AC008103, AL008715, AC003103, AC007326, AC006597, AF128525,
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					AC004805, AC006059, Z98050, AC016026, AL135744, AL109865, AC007156, AC005323, and
HBGMO31	15	997153	1 266	16 300	1000114.
HRGNW20	3	907090	1 421	15 426	A109/455, AWU/3155, A1690321, AA283204, A1739096, and A1968607.
KZW NDGD	77	709390	1-471	15 - 455	A1809990.
HBGOB07	53	883111	1 - 465	15 - 479	R15924, A1796491, A1346263, AA767342, AW173117, AW148990, AA860973, A1014603, A1640629 A1658566 AA506436 A1368262 AA768887 A1500714 A1365770 AA768887
					AI811626, AW081866, AA761573, AI683292, AI472126, S69381, AL008706, AF106657, and
					T66550.
HBGOJ28	54	967261	1 - 585	15 - 599	AW406518, R27278, W05444, W87344, AI159814, N56542, W87345, AA053475, AI905956,
2700001	,	2,070	,	,	153519, AW004657, AI743733, AA468421, AW001343, AA860298, and AA578670.
HBGOKS3	2	848156	1 - 621	15 - 635	AI459692, AW150902, AA781854, AI823723, and AC006255.
HBGOL08	99	958290	1 - 449	15 - 463	AA113287, D29499, AW294903, AW298373, AW297351, AW294452, Z40314, AI623657,
					D29192, and AI143487.
HBGPE04	57	926876	1 - 480	15 - 494	298049.
HBGPH02	28	918513	1 - 508	15 - 522	AI167166, AI034322, AA084622, AA457685, AI246080, AA448838, AI754291, AW243793.
					AI285521, AI816537, H55894, AC003037, Z97054, AC005913, AC006077, AL023879,
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HCDMB01	83	915613	1 - 430	15 - 444	AL042428.
HCDMB16	84	835781	1 - 261	15 - 275	
HCDMB60	82	726339	1 - 107	15 - 121	AI590413, AI869343, AI955933, AA593639, AI886450, AA576909, AI371486, AI971730, AA602301, AI421322, AI383426, AI371487, AW059533, AA858249, C00365, Z41784, F17104, AI200274, AW166558, AW337598, AA232052, AA280665, AA731352, AA729138.
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	1 - 202	1 - 116	1 - 490	1 - 1366	1 - 347	1 - 104	1 - 710
	954866	717671	934941	927904	932878	925748	651665
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	HCHOD89	HCHPO55	нсновое	HCMSE07	HCOMZ41	HC00G04	HC00107

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					H04750, T49622, AI219287, W02674, AA676625, AI961431, H02149, N27194, AA595296
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	1 - 221	1 - 251	
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	HLWBO68	HLWBQ84	HLWBQ86

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	1 - 271	1 - 448	1 - 532	1 - 886		1 - 310	1 - 343	1 - 519	1 - 632		1 - 824	1 - 261	1 - 530	1 - 688	1 - 412	1 - 439	1 - 38	1 - 384	1 - 545	1 - 703	1 - 600	1 - 943			
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	HLWBS14	HLWBS43	HLWBZ74	HLWCA67		HLWCM44	HLWCM70	HLWCO66	HLWCQ53		HLWCQ62	HLWCQ76	HLWDA01	HLWDB18	HLWDD02	HLWDE60	HLWDL71	HLWEE76	HLWFG82	HLWFQ04	HMVDU41	HNBTP01			

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	1 - 228	1 - 327	1 - 469
	965424	965428	933672
	321	322	323
·	HNBTT79	HNBTX52	HNBUM19

HNBUR07 HNGAO08 HNNNA06	324 325 326	951814 958685 917723	1 - 442 1 - 286 1 - 1581	15 - 456 15 - 300 15 - 1595	AC005829, AC002350, AL008582, AL135744, AL139054, AC006039, AC004991, AFÖ50154, AC004033, A1003147, AC005500, AP000557, AL049653, AC002310, AL031680, AC004662, AC004019, AC006509, AL049766, AL031311, AC005086, AC006285, AC004662, AC007540, AP0005501, AC0064812, AC004878, AL031311, AC00586, AC006285, AC006622, AC007540, AP000501, AC006821, Z97056, Y14768, AC006511, AC004841, AF024534, AC007283, AC007283, AC007281, AC006111, AC005811, AC007281, AC007281, AC007281, AC007281, AC006411, AC005261, AC006468, AC006512, AC007281, AC006481, AC005312, AC007211, AC005261, AL034451, AC005312, AC007151, AC005312, AC006511, AC0056611, AC005661, AC005664, AC005484, AL008718, AC006511, AC005664, AC006648, AC005839, AC006488, AC006664, AC006486, AC006488, AC006211, AC00571, AL034429, AC005666, AC004584, AL008718, AL031605, AC006597, AC005595, AF067844, AL022302, AC005996, AF129756, AC0065031, AF134726, AP001052, AC005944, AL022302, AC006992, AC006664, AC005894, AC005996, AC00699694, AC00699694, AC00699694, AC0069996, AC0069994, AC0069996, AC0069999, AC0069996, AC006999
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DININAUS	27/	91/124	1 - 548	15 - 562	AW069784, AI128373, AI128364, AI202042, AI143847, AI421235, AA779932, AI990994, AA143612, AI151527, AW194351, AA441818, AI275577, AA527080, AI278683, AA908252, W68235, AA855140, AI219401, AA676541, AW195552, AI299109, AI192236, AA862317, H01997, H56734, H82711, AA884790, H94868, AA774498, AA633305, H03629, T90526, AA904994, AI219227, AI567570, AI080080, R12503, R81669, W94691, H52108, AI444952, AA342086, H84426, W78812, N58039, W80711, H84425, R73007, H79700, H03628, and AI658795.
HNNNA77	328	917725	1 - 1103	15 - 1117	AW291524, H83578, AI202042, AA779932, AW069784, AA143612, AI128373, AI128364, AI143847, AA441818, AI219401, AI278683, AA862317, AA884790, AA633305, AA774498,

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HNOAS06	329	933730	1 - 738	15 - 752	AW183087, AA437061, AI992344, AI351831, AA423954, AI655434, AA029186, AI421314, AI025154, AA905377, AI189632, AI148753, AI971532, T77225, T77438, T53640, AA889771, AA029185, and N27393.
HNOAX12	330	969363	1-777	15 - 791	N59866, N22173, H24646, H27385, AL119324, AL1199457, AL042544, AL119399, AL119464, AW392670, AL119443, U46349, AL119418, AL134902, Z99396, AL119444, U46351, AL119391, AL119363, AL042965, AL119319, AL119395, AL119383, AW372827, AW363220, U46350, U46347, AW384394, AL119439, AL119497, AL119491, AL134538, AL119341, U46346, AL134536, U46341, AL134525, AL119335, AL043020, U46345, AL043019, AL042551, AP000473, AR066494, AR060234, AR054110, A81671, and AB026436.
HNOBF57	331	927903	1 - 769	15 - 783	A1672348, AW173697, AL079990, A1565451, AW305215, AA115462, AW081450, AW020072, AA031780, AA115214, AI094153, AI610893, AI088661, AI051834, AA233114, AA115204, AI469307, AI970462, AI620951, AW130820, N69772, AA495921, N34679, AA987696, AA495922, AA115067, AI770044, AI079994, AA150297, AI434100, AW236674, AI039432, AA951227, AI873440, AA938897, AI681115, AA031879, AA603790, AI301357, N44611, AA243692, AA377521, AA910225, AI913596, AI702644, AA961701, AW452143, AI352693, AI381836, AI767254, AI247300, AI050072, AI830541, AI865675, AI493755, AA573940, AA9337056, AI266405, AW138034, AA148788, AA653705, R37287, Z41281, AI090946, AI612953, AW103627, AA326653, AI572322, T49708, T49709, N85358, T49717, N84377, D25919, AP000300, AP000113, and AP000045.
HNOCQ04	332	964933	1 - 686	15 - 700	AI717999, AW404782, AI831040, C15687, AW410719, AI634938, AI479751, AA723194, AA398997, AA455667, AW410718, AI589849, AA584383, AI130687, AI190201, AI525790, AI460181, W69759, AA456685, AA632185, AA456287, AI298115, R53507, AA644652, D45471, AI368322, AW300844, AI762742, AA976082, AA621626, AI912458, AA781178, AA292406, AA643693, AI814720, AA399628, AI351664, AA989507, AW408212, AA132709, F20423, AA292771, AA765663, AA417936, AA026022, AI282190, AA394242, AA586966, AI351631, AA620713, AA582000, AI708099, R55785, AI039470, AI498903, AA132838, AA774256, N71139, AA777017, AA564894, AA635420, AI832846, AI203528, AI27498, AA774256, N71139, AA720518, AA552845, D81168, AA304523, AA582959, AA298391, AA838663, AA76543, AA411181, AA187606, AW404897, AA411255, AI814800, AA025235,

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HNOCU05	334	957833	1 - 733	15 - 747	AW364014, AW364012, AW364015, AW364019, AI760785, AI267509, AI224905, R80458, N76465, AI384093, NS9362, AA513728, AA729606, R80659, AI351352, AI499874, D61921, R69849. AA573139, R31977, and AR033047
HOCMU03	335	922418	1 - 602	15 - 616	
HOCPJ03	336	917484	1 - 299	15-313	AW374051, AW374048, AW374059, AA047322, AA573420, AA873293, H50745, T67156, and AI718619.
HODAD73	337	973463	1 - 490	15 - 504	AC004889.
HODAD95	338	974043	1 - 577	15 - 591	293783.
HODAG37	339	529410	1 - 224	15 - 238	
HODAH32	340	859509	1 - 305	15-319	AA076906, and AC004976.
HODAJ01	341	921666	1 - 570	15 - 584	
HODAJ35	342	529405	1 - 325	15 - 339	AC005618.
HODAK38	343	529404	1 - 310	15 - 324	
НОДАКЭ5	344	960179	1 - 690	15 - 704	A1333350, AI522314, N93898, AI539488, AI276544, AW292555, AA194179, AA193323, AA621456, and N64007.
HODA016	345	529401	1 - 271	15 - 285	
HODAT56	346	529402	1 - 354	15 - 368	
HODAV80	347	859519	1 - 287	15 - 301	
HODAW60	348	692684	1-315	15 - 329	
HODAW84	349	775425	1 - 503	15 - 517	AI800919, AI741507, N21056, AA969954, AA669258, AI018174 A1741491 and A1142521
НОДВС01	350	921662	1 - 290	15 - 304	1075071; min VIOLENTIA
HODBC07	351	954161	1-317	15 - 331	
HODBE01	352	921655	1 - 102	15-116	
норвн16	353	927781	1 - 286	15 - 300	
НОВВО85	354	859559	1 - 156	15 - 170	
HODBT58	355	678444	1 - 303	15 - 317	AA224807, AI355986, AI791718, C14330, AA778962, N94325, AA312559 H71678 H19817
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	529329	761447	967732	529400	932218	529327	967320	932638	529334	859556	573202	573200	573195	507249	529332	954149	917270	920698	524314											
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	HODBU95	HODBV71	HODCA11	HODCA68	НОДСД05	НОДСН64	HODCJ11	HODCJ42	HODCL88	HODCM62	НОДСО09	HODCO46	HODCO82	НОДСР69	HODCR43	HODCT07	HODCU01	HODCU02	HODCU62											

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	15 - 616	15 - 351
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	AI873627, AA504892, AW337526, AA910941, AA365318, R44855, AW381816, AA126271,
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·	HODET03	HODEV13	HODEX10		HODEY08			HODEY80	7	HODEZ11	HODFA38	-	$\dashv$	7	$\dashv$			HODFE69			9	ᅱ	HODFK18	

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CANTO TRADOCT STATEMENT	AAS34218, F29321, N28/49, A1192144, AA071339, AA137068, A1085091, N49765, H98947, W61183, and AF070668.	AW247757, AW239330, AA211149, AW249015, AW361739, AI557500, R18319, AF161479, AJ238379, AJ238742, AJ238741, and AJ238743	R80841.		W46445, W46513, AA179186, AA128660, AA804464, AW196128, AA583251, A1953806, AI872319, AI284510, AI610404, AI976755, and AI 133074	the state of the s	AA448573, AA252446, AA082102, W73318, AA339599, N24290, AA887226, R10417, AA037118. and U62940.			AW408436, AA403226. AW408309. AA323398. AA101050. and AI 050360	יייייייייייייייייייייייייייייייייייייי	AI276023, AI627898, AI539262, AI953242, AA947158, AA152216, T08709, H11221, and AC004126.			X07382, and Z28396.	AI432644, AI623302, AL134524, AI432654, AI432653, AW081103, AI432650, AI432677, AI431230, AI431307, AI431316, AW128900, AL045327, AI431328, AI431353, AI431312, AI431230, AI431307, AI431316, AW128900, AL045327, AI431328, AI431355, AI431312, AI4312655, AI431310, AI431354, AI431337, AI431239, AI431265, AI431246, AI431321, AI4312651, AI432661, AI432661, AL042898, AI431337, AI432651, AI432647, U46344, AL042508, AI431315, AI431330, AI431351, AI431248, AI431241, AA362690, AI868154, AA362689, T29199, AI061457, AI432662, AI431357, AI432655, AI431257, AL042853, AI431231, AI432662, AI431345, AI432658, AL042853, AI431257, AI431346, AL042853, AI431240, AI432645, AI432645, AI432645, AI432645, AI432645, AI432645, AI432657, AL042832, AI431314, AI268898, AI886152, AI492520, AI332600, AI282247, AI866786, AW129223, AI642488, RA2123, AI432643, AI932620, AI282247, AI642741, R43626, AI440238, AI643089, AI432655, AI64338, AI6430899, AI643089, AI	AL045328, R46015, A1431333, A1042420, A1047675, A1402500, AL045328, R46015, A1431333, A1042420, A1047675, A1402500, A1043420,
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		HOFMK22	HOFMM27	HOFMM72	HOFMN30	HOFMP31	HOFMP79	HOFMQ04	HOFMQ31	ноғмо65	HOFMS68	HOFMS74	HOFMS89	HOFMT20	HOFMT43	HOFMT66	

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	15-	15-	15-	15 -	15 - 404	15.	15-	15.	15-	15 - 343	15 - 447	15 - 409		15 - 444	15 - 226	15 - 282	15 - 275	15 - 166	15 - 426	15 - 378	15 - 363	15 - 407	15 - 516	15 - 396	15 - 226	15-416
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	563575	702492	744325	713809	859109	615287	792734	973354	658476	867984	727285	727173		716670	717067	859106	935569	715101	974435	708727	717355	666498	916963	906250	711205	770088
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	HOFMT72	HOFMU33	HOFMU63	HOFMU75	HOFMV84	HOFNA04	HOFNA92	HOFNC63	HOFND14	HOFND40	HOFND50	HOFND52		HOFND90	HOFND94	HOFNG01	HOFNG06	HOFNH33	HOFNI08	HOFNI48	HOFNI82	HOFNL18	HOFNL25	HOFNL37	HOFNL40	HOFNI.92

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869113	615305	705435	916588	973351	920218	715312	660317	859104	677372	683473	794308	935553	751692	827631	924473	606999				20000	/29399	947431
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15 - 402	15 - 839	15 - 443	15 - 492	15 - 209	15 - 563	15 - 781	15 - 885			15 - 286	15-713				
1 - 388	1 - 825	1 - 429	1 - 478	1 - 195	1 - 549	1 - 767	1 - 871			1 - 272	1 - 699			•, •	
954011	926098	575929	950216	575931	717068	209068	956896			961587	965013				
585	286	587	88 80 80	589	290	591	592			593	594				
HOGAU90	HOGAV36	HOGBF78	HOGCQ05	HOGCR32	HOGCT45	HOGCX95	HOGEE76			HOGEU49	ноологя				

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	1 - 203	1 - 409	1 - 360			1 - 346	1 - 263	1 - 305	1 - 475	1 - 1454			-										•				_			
	888442	727170	705406			858845	713792	858844	674177	970814									-					-						
	603	604	605			909	209	809	609	610							_									-				
	HOVBZ26	HOVCA52	HOVCD39			HOVCI76	HOVCI77	HOVCJ24	HOVCM22	HOVC011															•	•				

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	639	040	1 2 2	£ £	644	645	646			647	648	649
	НРОРО40	HPDQ005	HPDRD28	HPDRG92	HPDRO20	HPDVB07	HPDVE05			HPDVF03	HPDVK12	HPDVM06

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HPEAF19	651	867892	1 - 291	15 - 305	
HPEBA06		960802	1 - 242	15 - 256	AA299493, AI580853, AA303099, AI287555, AA299492, AI279700, AA559290, N71724, AF177861, AW338869, AA493503, AA367546, AL03177, AC006130, U73024, AC009509, Y10196, U63721, AC006333, AC004047, AJ012197, AL139054, AL050333, AC006544, AC004527, and D87008
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HPEBD31	654	655760	1 - 538	15 - 552	AA196263.
HPEBE44	655	716911	1 - 456	15 - 470	T72867, AA610577, and AC007695.
HPEKG18	959	914115	1 - 84	15 - 98	AF111167.
HPEKJ42	657	922391	1 - 214	15 - 228	
HPEKU27	658	921663	1 - 428	15 - 442	
HPEKX12	629	969251	1 - 355	15 - 369	AA737020, AW134485, A1874258, A1217712, AA935591, and AW389859
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HPFCA36	661	524720	1 - 275	15 - 289	AI798807, AC007065, AF073930, and AF064804.
HPFCA71	662	655596	1 - 351	15 - 365	
HPFCF09	663	236666	1 - 343	15 - 357	4 4 6 17057 41168222 4 CONSESS 4 CON
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					AL121658, AC005187, AC007279, AL080243, AC007546, AC006962, Z95113, AC005332,
HPFCF24	664	655744	1 - 398	15 - 412	ACU08372, ALU31387, and AL035249.
HPFCF40	999	009896	1 - 339	15-353	
HPFCF83	999	781490	1 - 329	15 - 343	AI749823, R99144, AA302658, AW161459, F24175, AI243793. AW161879, AI191343
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HPFCV71	681	525554	1 - 536	15 - 550	R31337, AW028647, and AF178081.
HPFCX18	682	655588	1 - 325	15-339	
HPFDD06	683	002096	1 - 291	15 - 305	AI557495, and AI557116.
HPFDE38	684	655704	1 - 343	15-357	AI417952.
HPFDE61	685	974249	1 - 681	15 - 695	
HPFDF79	989	973732	1 - 576	15 - 590	

		U73330.	AC004111,		AA593648.		AL079301, and AC004530.		AC005225, AL049835, and AL031297.	AW303098, AI061313, AI251203, AI251284, AI250552, AL046519, AI284543, T74524,	A1223626, HU/953, A1208841, A1254770, A1189682, AWU23111, A1826761, A1357823,	AIZS1034, AIZ49853, AAS/2813, AIS/5542, AI/55202, AI066646, AW410409, AA129/46,	A1732430, AA757661, AW276678, AI679759, AW149288, AI635819, AI355007, AW439703,	A1491765, A1753113, AW237905, A1149537, AA702637, A1864500, A1334443, AW192179,	AL038936, AA904211, AI587583, AA614214, AI247101, AL031730, AC002316, AL031311,	AL022328, AC007055, AL022326, AC006965, AL109865, AF109907, AC005081, AL034343,	AC005592, AL133485, AL049538, AL022238, AC005355, AC005011, AC007358, AC005291,	AL049540, AC008123, AP000688, AC004491, AL080243, AC008372, AL133445, AC003043,	AC004685, AC005874, AF134471, AP000501, AF111167, Z83844, AC004675, AL049780,	AF088219, AC006552, AJ011930, AC007277, AC005330, AC007243, AC006046, AC004686,	AC005363, AC005209, AC005231, AC005746, Z97056, AL135960, AJ131016, AC004883,	AC005619, AC005189, AC002430, AP000511, AL032821, AC006213, AF134726, AC007384,	AC006130, U91326, AC002544, AC004084, AC004067, AL121603, AC005519, AC005899,	AC004821, AF031078, AC008064, AJ010770, AC002369, AF030876, AC009731, AC005844,	AC009510, AL031228, AC005406, AL079352, AC005884, AL022721, AL022476, AL049795,	AC004879, AC005821, AL049760, AC005234, AC004593, AC007129, AC016830, AP000031,	AL023284, X55927, AC006960, AC006203, AC005911, AF001548, AC010202, AC005368,	U07563, AC004542, AL096701, AC006241, Z98759, AC005015, AC004656, AF015416,	AF001549, Z82171, AC002350, AP000134, AP000212, AP000030, U91325, AC007385,	D84401, AC002404, AC007637, AC006511, AC006480, AL031803, AC005606, AC002347,	AC000115, AC005829, AF031076, AL031281, AF053356, AC004051, AL096791, AC005072,	AL049758, AL133353, AC005565, AC016027, AC003101, AC005531, AC004990, AF001552,	AL121652, AC004517, AL117351, AC007011, AC004033, U95742, AC003109, Z70280,	Z83845, AC004147, AC007216, AC004805, AC006079, Z84470, AC005747, AC005225,	ABUZZJU46, ACUUSUS, ACUUSIJU, ACUUSIZO, ACUUSIZO, ACUUSIZO, ACUUSIZO, ACUUSIZO,
15-324	15 - 369	15 - 207	15 - 281	15-373	15 - 324	15 - 359	125-31	628 - 51	125-371	15 - 694																									
1-310	1 - 355	1 - 193	1 - 267	1 - 359	1 - 310	1 - 345	1 - 357	1 - 365	1-357	1 - 680																									
655610	655549	954333	655543	581133	655530	974569	522113	867879	739617	867870					-											•									7
189	889	689	069	169	692	693	694	695	969	269																									
HPFDG58	HPFD123	HPFDL90	HPFDS59	HPFDT17	HPFDT54	HPFDT61	HPFDU30	HPFDU38	HPFDU59	HPFDV71																									

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					AB016897, AC005921, AC002300, AL034374, AC004125, AC009247, AL021808, AL008723,
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HPFDX13	869	655571	1 - 641	15 - 655	W67821, AI934358, AW183528, N55430, AW008575, W67636, AA825800, and N55148.
HPFDZ20	669	655764	1 - 328	15 - 342	
HPFEA08	700	960372	1 - 386	15 - 400	<b>Z82203.</b>
HPFEA32	701	925499	1 - 295	15 - 309	
HPFMA06	702	953536	1-213	15 - 227	AISS9365, N40914, AI275689, AI769835, AI935795, AW016872, AA528426, N90231,
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				•	A1768580, A1689518, AA570675, AA374175, W37740, AA594795, AW088741, AW197140,
					AA165407, AA165437, AA604629, AI744021, AA780710, AA581888, AA722100, N66617,
					N30750, N25542, N26634, D61746, AI364247, AI363458, AI719503, Z39345, AA165599,
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					AI695775, D51138, H89566, AI828511, AI423935, D19831, AI364605, R38667, AA461285,
					D51197, AI913698, T62947, D62512, AA063398, AI766125, T31394, AL133241, AL009179,
					and AC008126.
HPFML02	703	917775	1 - 102	15 - 116	AI535639, Z33559, Z32887, T18597, AI541356, C14228, D59751, AI557864, D50992,
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					AI557082, AI557474, AI525302, AI525500, AI525556, AI557533, AA058620, AI557317,
	_				AI525316, AI557809, AI541075, AI557155, H65400, AI541321, AI541365, AI525757,
					AISS7312, AISS7602, AIS57731, AIS2S852, AIS25661, AIS41353, AIS41034, R29657,
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AI540974, AI546829, D30843, AI535828, AI557543, AI535813, AI536070, AI535994, AI557039, AI541154, AI547177, AI557041, AI557408, AI541027, AI541048, AI557154, U45328, AR050070, A62300, A62298, A82595, A82593, U94592, Z30183, AF006072, and AR025466.					AA195825, AA306492, AA418582, C16647, AW160459, AA309024, AA308183, AI571333.	AA738174, AA195976, AI570688, AA612815, AA995713, AA418567, AI376546, AA977055, AW162470, AA575997, AA083678, AA100585, R35954, AA643289, AI566298, A1094772.	F00910, A1282111, AA492519, A1564065, AA676682, AA622171, AA378734, R35925.	AA884373, AII38493, AA156573, AA111863, AI305825, AA553893, AI557187, AA618507,	AA469352, AA159175, AI266155, AA469274, N74960, AA412547, W05658, N39508,	AA658912, AA083301, AA328913, F26029, AF088991, AF044954, AF067169, AC005363, AC005606. X63224, AF088992. and AF088993.		AA312500, AA354863, AA319616, T69203, AA491370, H16422, AW403746, and AL031427.		AA101561, W76302, C17760, AA227408, AA215609, AA101519, AA626769, AA359412,	173740, A1227392, AF111713, A91701, A91699, AF207907, AF172398, AF134005, and   AB017568.				R43644, AA953944, and AL035454.	AA741301, AA331014, AA461592, AI300413, AI342786, H42893, AI302277, AW407007,	AI018726, AW157173, AW162314, AW162332, AW168699, R71796, AA657910, AJ818313,	AA423461, AA025008, AW0820/6, ALU41/33, A14/1455, A168/343, A14/36/1, A1963816, US6670, A A226000 MINOR TARGET A A018600 A A01860 A	11002/77, KAZESZSZ7, IISOSZ96, IISOSZ66, AMULOSZS, AMULOSZS, ALZSOL4S, A1439806, AA643451 AI 037006 F35902 AI679759 AW193414 AA084505 A1474085 A1476186	AI925462, AI440243, AA092862, W45457, AI951112, AI620045, AI183426, AA225630.	A1167360, H99222, N21300, AA992562, AW190925, AI936229, AW080772, AA829669,	AI376239, AI017733, AL039117, AA381880, AW105346, AA112864, C14599, F26285,	AA587536, H27788, AA904211, AA827383, AW019964, AW262466, AI799260, AI860535,	AA400660, AA64341, A1902030, A131/2/1, AA604149, A133835/, A1032411, A1131261,
	15 - 396	15 - 427	15 - 438	15 - 61	15 - 464						15 - 225	15 - 610	15-314	15 - 425		15 - 468	15 - 440	15 - 435	15 - 414	15 - 205								
	1 - 382	1-413	1 - 424	1 - 47	1 - 450						1-211	1 - 596	1 - 300	1-411		1-454	1 - 426	1 - 421	1 - 400	1 - 191								
	655748	655595	919469	655573	928614						615007	925424	655753	884289		725539	625719	655757	786117	655540			,					
	704	705	706	707	708						709	710	111	712		713	714	715	716	717								
	HPIAE79	HPIAO83	HPIAQ49	HPIAQ76	HPIAS40						HPIAV80	HPIAX11	HPIAZ37	HPIBQ37		HPIBR51	HPIBT49	HPIBY65	HPICC89	HPJAB19								

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HPJAB84 71	718 6	655531	1-314	15 - 328	ACCOULECT.
HPJAC36 71	719 6	655601	1 - 401	15-415	A1167181
HPJAC92 72	720 8	867831	1 - 338	15 - 352	

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AL080239.	283851.	AI979243, and AI967993.		T93943, T93893, AA399372, and T81024.		AC006071.	AW275406, and AC000378.			AF108195, AF159714, AF186379, AF106698, AB025784, and AF040330	10000 training (1000000)	T08031, and AB011095.	AP000494.	AC005923.					AI133297, AW163293, AW303196, AA191659 AW080777 AW084466 A1400588 A A 220421	AA548890, AA431949, AA486131, AW301350, AA457070, H71479, AI040142, AW275510	H52274, AL133909, H82316, AI250083, AA661921. AW102846. AI 042470. A1051775	AA476397, AI766906, M77893, AA630672, AI205010, AI284640, AI 038498, C18550	AA320966, AA579179, AI393931, AA114983, AA774780. AL119713, A1002720, AW274349	AA508359, AI818231, AI271164, AA838190, AI806102, AA577824, AA385798, AI708009	AA578327, AI889566, AA832188, AI499301, AI801482, AI298061, T92347, AW103927	AA984295, AA558884, AA055871, AI733755, AA584876, AA504877, AA127426, AA669155.	H09071, AI805363, AI203925, N23504, AA101689, AW104793, AI168167, AI694130	AA572971, AI950983, AI056913, AI345157, AI924872, AW316873, AL046689, AA653857.	AA323701, AA772851, AA526787, AA778992, R64559, R95448, AA490183, H49568,	AW022897, AA402129, AA493695, AA834707, AA738253, AA719073, T99179, AL035209.	AL035450, AC000119, AC002529, AL133371, AC002310, AC007446, AC007845, AC002127.	AJ003147, AC007652, AL031053, AC005215, AC003100, AC004638, AC006314, AL033523,	AC002416, AC006466, AC006112, AC006312, AC005998, AC004745, U57009, AL049773,	AL049/33, AC006989, AC012599, AL035608, X53548, AC004161, X54175, D83989.
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1 - 329	1 - 276	1 - 237	1 - 321	1 - 757	1 - 417	1 - 69	1 - 249	1 - 351	1 - 286	1 - 357	1 - 421	1 - 325	1 - 333	1 - 535	1 - 320	1 - 337	1 - 218	1 - 171	1 - 278															
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721	722	723	724	725	726	727	728	729	730	731	732	733	734	735	736	737	738	739	740															1
HPJAD09	HPJAD66	HPJAD82	HPJAV07	HPJAW56	HPJB117	HPJBI89	HPJBK52	HPJBU08	HPJBV17	HPJCC04	HPJCP10	HPJCP11	HPJCS84	HPJCV50	HPJCX15	HPJCX26	HPJCY70	HPJCZ03	HPJCZ06													•		

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	15 - 643	15 - 556
	1 - 629	1 - 542
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	749	750
	HPJEQ22	HPJET90

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	1 - 504	1 - 488	1 - 278
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HPLBL31	755	503732	1 - 349	15 - 363	AA368423, and AA368422.
HPLBL57	756	503730	1 - 261	15 - 275	AA303008, AA303009, and AC002427.
HPLB061	757	558187	1 - 229	15 - 243	AA368593, AA758725, and D86985.
HPMAG19	758	705471	1 - 290	15 - 304	AA369206, AA369215, AW276918, AI498304, AI859717, AI635381, AI873828, AI806367,
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HPMAH75	759	766443	1 - 301	15-315	AA303039, AA369332, AA335519, AA553332, AA745302, N63749, Z95331, AC003682,

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	1 - 416	1 - 489	1 - 106	1 - 349	1 - 431	1-415	1 - 470	1 - 195	1 - 372	1 - 332	1 - 428	1-211	1 - 403	1 - 301	1 - 266	1-416	1 - 275	1 - 393	1 - 241	1 - 291	1-319	1 - 195	1 - 120	1 - 429	1 - 630	1 - 190	1 - 300	1 - 344	1 - 325	1 - 637	1 - 290	1 - 340	1 - 192	1 - 285
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	HPMBK49	HPMBM48	HPMBN02	HPMBO10	HPMB061	HPMBR17	HPMBU81	HPMBX35	HPMBX79	HPMBY76	HPMBY83	HPMBZ05	HPMCB65	HPMCC73	HPMCD77	HPMCI02	HPMCI65	HPMCJ14	HPMCJ19	HPMCJ48	HPMCK65	HPMCS19	HPMCS65	HPMCV93	HPMCW25	HPMCW53	HPMCX11	HPMCY30	HPMCY31	HPMCY35	HPMDJ09	HPMDL78	нРМD039	HPMDR07

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1 - 334	1 - 313	1 - 39	1 - 360	1 - 397	1 - 299	1 - 333	1 - 270	1 - 438	1 - 428	1 - 323	1 - 140	1 - 704	1 - 391		1 - 327	1 - 648	1 - 220									•		_					
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HPMFB84	812	577593	1 - 347	15 - 361	U40369. AA917042, AA476820, AA861762, AW197737, AA883969, AI2222281, AI394043, AI476496, AI420953, AI816942, AW418714, AI337319, AI312584, AI268413, W60319, H72483, AI125256. AI198189. AI739036. Z57770. Z59847. and Z57771.
HPMFE35	813	577633	1 - 415	15 - 429	AC005909,
HPMFE60	814	577636	1 - 309	15 - 323	17 000001 1 1 0000000 1
HPMFH21	918	575943	1 - 447	15 - 450	ALMUSUSI, and ACMUZSZO.
HPMFJ50	817	575932	1-475	15 - 489	R20682, T65200, Z44442, and F11983.
HPMF155	818	577588	1 - 369	15 - 383	
HPMFL08	819	692626	1 - 452	15 - 466	AA555286, AA640814, AI281916, AW073979, AI378363, R70468, AW242350, AW013856, AA644290, AW449140, 293016, AC012384, AL035541, AC005228, AC003662, and AC009300.
HPMFL80	820	874359	1 - 440	15 - 454	AA313895, AA834888, AA362291, AW366931, AA436945, AA496034, AI834310, AA402490, AI039687, and AC004841.

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AA255639, R53909, AI492887, H09275, AW192355 N48979, and AI 117598			AC008072.	AC006121.	R31294, AI823535, AI823533, AL038977, AW271095, AI252141, AL135383, AI792856, AA594742, AW302832, AA828911, AI284536, AI251503, AI73946, AA578905, AI833596, AI732593, AL022695, AI792746, AI792842, AI252190, AI281401, AI689198, T56025, AA551907, AL689128, AA651067, AI884861, AA169245, AA694047, H81918, AI798313, AI298660, AI038324, AA551067, AI884861, AA169245, AA694047, H81918, AI798313, AI298660, AI038324, AI798569, AI866786, AA169779, AL034420, XI4448, AL021978, AC007731, AC005000, AC005031, AC006051, AC006071, U78027, AC015853, AC005932, AC006333, AF001549, AL035422, AC006071, U78027, AC004000, AC005037, AC005828, AS59908, AC004771, AC006088, AL133243, AL039081, AL031573, AC0052071, AC005204, AC006263, AC004602, AC006051, AC005204, AC006088, AL133243, AL037071, AC006087, AC005204, AC006088, AL133243, AL037071, AC0060926, AL031334, AC004821, AC004821, AC004821, AC004821, AC004821, AC004821, AC005290, AC005294, AC005294, AC004821, AC004821, AC005290, AC005294, AC005294, AC004821, AC004821, AC005291, AC005297, AC005791, AC0050926, AL135744, AC004821, AC005290, AC005294, AC005294, AC004821, AC004821, AC005294, AC004821, AC00497, AL035398, AP000024, AC004941, AC004812, AC004821,	295331.	
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582595	968821	867662	577629	575914	867651	711640	916662
821	822	823	824	825	826	827	828
HPMFM29	HPMFN12	HPMFP05	HPMFP30	HPMFP38	HPMFQ84	HPMFS41	HPMFT04

	AA434145, AI422195, and AC007239.	AL120663.	R56205, N31111, AW403866, and AA338327.		C18404.	AI245605, AI733581, AW195539, AA994974. and AI.050350	AL031282,	AC005383.	AL008730.		Z85999.	AI214759.	AA309957.			AA034305, AI752781, W38450, AA295920, W69345, AW368627, W01351, AW167099	AA491113, A1093592, AI628843, AA470016, AA459627, R70436, W16698, H30472, R72510	R27103, A1986035, A1926603, H25748, AA432254, W67475, R53035, AA617710, AA865403	AA412294, AA431234, AA514353, AI002434, W69267, R37917, R24912, AA443912, H24995.	R72497, and X52574.	AC006960.		AA308643.		AA361434.		W51873, AA215789, AA215316, AI654057, AI809466, AI761738, AA292627, N24002.	AI860134, AA279010, AA215628, AC003032, and Z56178.	R82057, and AI828591.	AA702486, AI630976, AW339792, AW418628, AI690212, AI350097, AA830893, AA703551,	AJ458500, AA936420, AW402861, and AB020714.	AL050074.	AW409684, T06413, AB003151, AP000688, and AB033064.	
15 - 340	15 - 344	15 - 377	15 - 367	15 - 280	15 - 480	15 - 450	15 - 355	15 - 360	15 - 362	15 - 526	15 - 322	15 - 381	15 - 435	15 - 436	15-810	15 - 565					15 - 369	15 - 416	15 - 401	15 - 283	15 - 361	15 - 428	15 - 506		15 - 531	15 - 662		15 - 356	15 - 394	15 - 113
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575894	652097	575911	956263	960065	932529	575908	867657	577642	577603	968359	506379	920313	703835	867648	873392	954823					577615	577641	924521	920326	864040	575924	671936		730751	854081		577599	506235	575951
829	830	831	832	833	834	835	836	837	838	839	840	841	842	843	844	845					846	847	848	849	850	851	852		853	854		855	856	857
HPMFU89	HPMFV28	HPMFV82	HPMFV88	HPMFW25	HPMFW78	HPMFX13	HPMFX65	HPMFX70	HPMFX92	HPMGA83	HPMGB22	HPMGC07	HPMGC23	HPMGE31	HPMGE95	HPMGF06					HPMGF32	HPMGH16	HPMGI03	HPMGI84	HPMGJ93	HPMGK37	HPMGK59		HPMGK62	HPMGM33		HPMGM54	HPMGR80	HPMGS09

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				AW242577.		AI806968, AI080168, AI207589, AB006572, and AF091095.	AL133605.	H09672, and AI937462.		AL008709, and AL020990.	AI247199, AW166611, AI254913, AA833896, AA833875, AA644090, AI818737, AL048466	AW069227, AI460050, R81017, AA613624, D44639, AA603530, AA307598, AW270385	AA634786, AI682665, AA468022, AL047349, AI687343, AI753113, AA528390, AW302017	AA707849, AA984187, AI925579, AA526724, AI084348, AI278972, AI 040054, AI791150	AI867058, AA580808, AA633920, AW188742, AI634187, AI5374458, AI004591, AA27400	AA639946, AA574442, AI591375, AA643770, H63092, AW305371, AA651632, AA837035	AA558560, AA862179, AI216990, AW270256, AA846959, AA871247, AI908003, AA876040	AA084609, AI469577, A1049955, A1720195, AW131043, A A314801, A A355024	AA48 1887 AI737869 N73013 AA101418 A165770 ANNORMS AA450007 HISES	AI283312. AA176605. AA846944. AA904775. AA704363. NE4587. AA834777. AA515779	AA601356. A1457313. AW440545. A157157. NADDOO FROISS. A A402726. A A 264462	AA583394 AI537020 AA790975 AA671323 AI34127 AA83741 WOLDER A AICENCY	AIS80707, AW265138, AA521399, AA086418, A1344948, AA36749, A130094, A150096,	AA806796, AA721645, AC000025, AC004796, AC005736, AC005081, AC005899, 178810	AB026906, AC005581, AC004382, AL133448, AC006241, AC004000, 1196629, AL 1086703,	Z98884, AL133245, AL035685, AC006077, AC005844, AC004098, AC007227, AC004876	AC005746, AC004686, AL078604, AL033517, AL023807, AF196969 799755, AC005180	AC005800, AC016025, AL022313, AL132777, AC004253, Z97181. AC004881, Z82172	AC004973, AC004890, AC002110, AL079305, AC003663, AL132985, AC005632, AC006047	AC004019, AL031846, AC007327, Z84482, AP000313, AC002104, AC004913, AP000299	AC005102, AC004447, AC005725, AC000120, AC007666, AP000066, AC006014, Z71183	AC004476, AP000193, Z99716, U62293, Z93023, AC005619, AC000052, AI.034429	AC005089, AC006441, AL031311, AC005783, AL080243, AC010170, AP000050, AF053356.	AL024507, AF134726, AL035494, AC005768, AL031662, Z83844, AC005231, U47924,	U41193, AC005740, AF111169, Z81364, AP000117, AP000269, AC005920, AC006197.
15-368	15 - 125	15 - 302	15 - 275	15 - 278	15 - 442	15-315	15 - 296	15 - 553	15 - 378	15 - 371	15 - 443																								
1 - 354	1 - 111	1 - 288	1 - 261	1 - 264	1 - 428	1 - 301	1 - 282	1 - 539	1 - 364	1 - 357	1 - 429		•		_	_	_																		
796440	970815	968364	582596	577635	650306	575903	970813	577595	531382	577631	928433													_								_			
858	859	860	861	862	863	864	865	866	867	898	698																								
HPMGS24	HPMGT67	HPMGV12	HPMGV15	HPMGV59	HPMGW48	HPMGX23	HPMHA80	HPMHB74	HPMHB83	HPMHC74	HPMHD66																								

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	·				Augussay, 11/104, AADS4968, AUSTS49, AAU/1144, AAJ09841, AW/11040, AID1172, AA43448, AI679706, T07287, AA601876, AW072923, AI35812, AI205084, AA817722, AA43448, AI679706, T07287, AA601876, AW072923, AI35812, AI205084, AA071393, AG005397, AC004990, AC005829, AC006837, AC005398, AC005397
HPMJN59	877	946876	1 - 547	15 - 561	AA278625, AL043338, AA417787, AI917735, AW303607, AI819365, W23045, AI243857, AA157110, and AA278626.
HPMJO46	878	922649	1 - 293	15-307	
HPMJR02	879	917419	1 - 505	15-519	AC005406,

	AC006443.	H66737, AA610385, AI825101, and AC006453.		AW130066, AI826186, AW150146, AA129308, AW392049, AA129351, AA453884, AI278397, N24006, AA453799, AI796331, AA336728, N74882, AW380924, AA369050, AI868063, AW131507, AC004774, D31734, AF033011, U67840, L24443, AF022075, AF022077, AF022076, U25274, AF096161, L09729, U03876, Z63754, and Z63755.	AA457012, and AC002310.	N89001.	AA848128, and Z93244.		R66945, and AI090443.	771183.		A1097067, A1383144, AA370038, and AC005746.	AA370352, AA370860, AA024451, AL118518, AC007016, AF064859, AC004707, Z84718, and AP000351.	AA370859, AA370351, AC002536, and AL034371.	AA398734, AA393413, and AA371065.	AA371132, AA371091, AW270853, AI978920, AI468384, AI971306, AA361429, and AC005156.	AA371242, AA757085, and AI018367.	AA370885, and AC002366.		AC007198.	AA298484,	AA370278.		AC002352.		AA370571, and AI905054.	AA369901.	A1925663, AA458636, AA193435, AA252059, W94787, AI470629, AW016321, and AA193532.
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958001	759226	969478	166156	894416	867573	867533	918123	922621	690856	7£0£96	509490	259176	585489	536630	968692	655537	655587	655693	960316	655725	939490	964909	655554	968521	666295	849081	192807	967944
088	881	882	883	884	885	988	887	888	688	890	891	892	893	894	895	968	897	868	668	006	901	905	903	904	905	906	206	806
HPMJV08	HPMJY55	HPMKB19	HPMK153	HPMKM81	HPMKN43	HPMLE04	HPMLK02	HPMLK76	HPMLL74	HPMLW10	HPMSF86	HPRAE13	HPRAN84	HPRAU45	HPRAZ10	HPRBA65	HPRBE36	HPRBL91	HPRCB11	HPRCB21	HPRCC08	HPRCC61	HPRCN41	HPRCU13	HPRSB16	HPRTL26	HPRTP73	HPVAB11

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	AI584019, and R79760.	AA296794.	. U18010, A1699466, and L77587.		AW139964, W81697, AW088477, AI887846, AA447817, AA447667, AA677404, R93353,	AA831618, AA574189, AI124782, AA584550, AA055366, F13631, AA765804, AW268271,	AA993918, AA679335, AC008173, AC004074, AF146367, AF124523, AF118808, AL096775,	AL109954, Z83841, AC002464, AC005820, AC006048, AP000509, D84394, AC007359,	AC008175, AC006499, AL136130, AL096801, and W81696.		T65635, AI354862, AA017323, H48816, AI187056, AA829490, AA507745, T47324,	AA548692, H91844, AA565232, AA640022, T08163, N22395, AA524604, AA524829,	AA373304, AI818505, Z83844, AL031255, AC012384, AC004408, AC006449, AC002996,	AC004149, M89651, AC005529, AC004491, AL031228, AC002357, AC002425, AC004531,	AC004947, AC005837, AC004051, AL049779, U52112, AL132774, AC004690, AC005225,	AC006162, AC007686, Z69303, AC006006, AC004231, AC005323, AL136295, AC002511,	AF107045, AC006077, AC004596, AL050317, AL022324, AC006275, AL080245, AL035427,	AL031053, AL049776, AL024507, AC005399, AC004682, AP000688, AC002375, AL078476,	AL121825, AC004552, AC005839, AC007052, AC005527, AL049829, AC007055, AC003049,	AP000555, and AF124730.	AI075673, and AC008015.			T20053.	AW338702.	AW080827, AI535841, AC002038, AC002041, and AC006352.	H68009, AA532955, and AC005189.			AA300733, AW070249, and AC000089.	AW264269, AW028491, AA424983, AA418896, AA418895, AA460211, AI800304, AI685341,	AI188340, AI160534, N26011, AW057810, and AI917673.	R59356, F10756, AA480322, AI768068, T15624, AI760446, AI870727, AA534696, AA679825, AI868057, AI274320, AA716748, AI922465, and AA907744.
15 - 426	15 - 429	15 - 493	15 - 620	15-157	15 - 739					15 - 227	15 - 344										15 - 368	15 - 358	15 - 381	15 - 486	15 - 657	15 - 254	15 - 542	15 - 343	15 - 255	15-410	15 - 799		15 - 152
1-412	1 - 415	1 - 479	1 - 606	1 - 143	1 - 725					1 - 213	1 - 330										1 - 354	1 - 344	1 - 367	1 - 472	1 - 643	1 - 240	1 - 528	1 - 329	1 - 241	1 - 396	1 - 785		1 - 138
655578	753744	525537	655691	655527	908450					655733	867289										657484	655614	655560	655577	514113	961529	537333	655713	655591	710354	705322		785439
906	910	911	912	913	914					915	916										917	918	919	920	921	922	923	924	925	926	927		928
HPVAF49	HPVAF69	HPVAH36	HPWAF85	HPWAH48	HPWAS77					HPWBA33	HPWBO84										HPWCA53	HPWCJ27	HPWCJ67	HPWCJ82	HPWDA73	HPWDA86	HPWDD72	HPWSB35	HPZAB38	HSWAC73	HSWAD39		HSWBD86

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711066	868007	923070	537136	504353	961232	835805	537271	787500	69/985	-			963538		966113	783328	927010	062629	702441	887787	967959	779134	779265	742218	693377	953904	
929	930	931	932	933	934	935	936	937	938				939		940	146	942	943	044	045	946	947	948	949	950	156	
HSWBJ40	HSWBO34	HTEAA54	HTEAB52	HTEAD32	HTEAD95	HTEAF07	HTEAF26	HTEAG50	HTEAK57				HTEAL28		HTEAP91	HTEAR84	HTEAV43	HTEAY67	HTEA754	HTFRC74	HTEBD35	HTEBD40	HTEBJ78	HTEBP39	HTEBS30	HTEBS77	

AA399558.	AL133028, and AB033037.	M78063, AI560292, H50301, AA340759, AA340760, H45375, 1109355, and AE096153		AB033083.		AA725713, AL040570, R48431, and AC020663	AF193806.	AA382976.	AI017997.	R20356, H09898, and R13239.		AI479803, R89200, AA382300, AA700729, and AI 035450				AI521186, AI287890, AW006015, AI739342, AI536021, AI915154, D59412, AI382968, AA723799, C14160, and B 58305		AL042436, AI125824, AA437087, AI028669, AI024321, AW241753, AA400083, AA953011, AA97296, AI674705	AW375961, H12646, N46186, A1114644, AA133382, AA314676, TO2864, AA482645	AA203566, W20194, AA878228, W80608, AA699466, AA482495, Z25122, AA490161, AA939181 A1635552 and AF13561	AL079435, AW070333, AA868621, AI024608, AI208541, AA644440, AA992264, AI219709,	and ALU/8621.	AA219332, and AW274715.	AL039822.	268165.	T36107, T19204, AF012359, and T36109.	AL079683, T69495, AA377984, AA411067, W19966, AL135463, AA152011, A1080369	A1928496, A1969686, AW150086, AW162108, AW245409, AW245596, AW087350, A1660688,	AW0233/0, AL986318, AA417624, AW073180, R65681, AA609692, AI568566, AF015913, and AF167572.	
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854052	508150	960427	526281	923026	711523	967340	958381	507053	764416	911369	947605	708860	870692	921070	971673	963353	508143	844558	790937		796820	500130	208138	9598/4	508108	973163	518124			
952	953	954	955	926	957	928	656	096	961	796	963	964	965	996	296	896	696	970	971		972	,,,	2/2	9/4	975	976	116			
HTEBS80	HTEBX62	HTEBY08	HTEBY15	HTEBY28	HTEBY41	HTEBY61	HTEBZ21	HTECA13	HTECA16	HTECA21	HTECA32	HTECA51	HTECA83	HTECB21	HTECC13	HTECC20	HTECC37	HTECC38	HTECC66		HTECC80	UTECCOS	HIECCOS	HIECCYO	HTECD17	HTECD18	HIECD36			27 000 000

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727422	620494	764830	790894	522983	522984	522964	522966	964734	522973	925527		761752	522764	522765	957762	921243	932292	536477	519940	771404	960303	870711	530592	964379 1	870675 1	870548 1	839532 1	536821	530589 1
979	086	981	982	586	984	985	986	286	886	686		066	166	365	993	994	995	966	266	866	666	1000	1001	1002	1003	1004	1005	_	1007
HTECD75	HTECE09	HTECE44	HTECE45	HTECE69	HTECE91	HTEDF13	HTEDF23	HTEDF57	HTEDF76	HTEDG16		HTEDG34	HTEDH21	HTEDH22	HTEDH54	HTEDI02	HTEDI16	HTED182	HTEDJ04	HTEDJ30	HTEDM08	HTED031	HTEDOSI	HTEDO59	HTEDP15	HTEDP31	HTEDP32	HTEDP83	HTED030

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1010   761585   1-303   15-507     1011   530451   1-363   15-377     1012   870708   1-1168   15-1182     1013   932315   1-718   15-732     1014   921114   1-152   15-166     1015   523959   1-552   15-566     1016   530452   1-345   15-359     1017   771505   1-128   15-142     1018   922964   1-845   15-859     1010   530580   1-314   15-328     1011   530580   1-314   15-347     1012   924818   1-601   15-615     1022   924818   1-601   15-615     1023   968517   1-327   15-347     1024   530157   1-372   15-347     1025   524840   1-314   15-388     1027   524850   1-314   15-388     1028   530199   1-314   15-389     1029   698315   1-315   15-485     1030   960127   1-471   15-485     1031   523957   1-298   15-312     1033   530095   1-134   15-148     1034   935982   1-210   15-224     1034   935982   1-210   15-224	2000	200	705063	1 - 405	1/4-CI	AA424209.
1 1010       761585       1 - 303       15 - 317         1 1011       530451       1 - 363       15 - 377         2 1012       870708       1 - 1168       15 - 1182         8 1013       932315       1 - 718       15 - 732         2 1014       921114       1 - 152       15 - 166         2 1015       523959       1 - 552       15 - 566         2 1016       530452       1 - 345       15 - 328         3 1017       771505       1 - 128       15 - 341         4 1018       922964       1 - 845       15 - 859         7 1019       530580       1 - 277       15 - 241         8 1020       925399       1 - 227       15 - 551         9 1022       924818       1 - 601       15 - 551         1 1023       968517       1 - 373       15 - 347         1 1024       530580       1 - 373       15 - 346         1 1025       924840       1 - 373       15 - 369         1 1026       507814       1 - 279       15 - 369         1 1026       530199       1 - 314       15 - 369         1 1027       524059       1 - 314       15 - 369         1 1030       960127	2000	5001	230280	1 - 493	15 - 507	
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5         1016         530452         1-345         15-359           8         1017         771505         1-128         15-142           4         1018         922964         1-845         15-859           7         1019         530580         1-314         15-328           8         1020         925399         1-227         15-241           9         1020         925399         1-227         15-241           1021         523962         1-537         15-551           1022         924818         1-601         15-615           1023         968517         1-333         15-367           1024         530157         1-372         15-336           1025         924840         1-333         15-338           1026         507814         1-279         15-338           1026         507814         1-355         15-369           1027         524059         1-331         15-369           1029         698315         1-355         15-369           1030         960127         1-471         15-485           1031         523957         1-298         15-312           1032<	EDX22	1015	523959	1 - 552	15 - 566	T64832, Z45475, and F12119
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1030         960127         1-471         15-485           1031         523957         1-298         15-312           1032         917206         1-862         15-876           1033         530095         1-134         15-148           1034         935982         1-210         15-224						AL035461.
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1033   530095   1 - 134   15 - 148   1034   935982   1 - 210   15 - 224	EW73	1032	917206	1 - 862	15 - 876	AI125404, AI247364. AI208217. AA910021. AI915307. and T11405
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AL137385.				AL080239, and AL030997.	AI733211, AA977235, and AI793144.		Z84469.		Z20330.		AA416708.		AA304950, and AC005237	AA861754, AI041049, AA974148, AI025824, AI015271, AA973722, A1262750, AF012394	H44966, H45019, H65081, H65127, H65128, H65081, N30790, N32825, N41565, A A021000	AA037708, AA158991, AA158990, AA552704, AA581540, AA583387, AA594383, AA568601	AA639650, AA962753, AI076864, C01177, C17452, AA610069, AA677739, AA678002	Z17891, Z17844, Z17858, D29489, D31204, D31401, D31430, A1147272, A1348141, A1434148	AI446782, AI401705, AI473505, AI475244, AI560742, AI565331, AI479120, AI567547	AI569204, AI570723, AI571642, AI521092, AI587097, AI619824, AI619826, AI683822,	AI745345, AI700348, AI862997, AI891040, AI805378, AI805561, AI814808, AI917522	AI924990, AI925791, AI925824, AI926709, AI932677, AW008971, AW025107, AW028154	AW028895, and AW044371.		AA469976, and AA382993.	AI739081.		AA320491, AA461257, T96959, AA620998. AI803092. AI598264. AIR07911. AA613500	AI701066, AA873354, AA976002, AI337726, AI401363, AA889162, AW449691, AA460950	AI435494, T91835, N47591, T08650, AI672896, AI015106, AL122076, AF082179, AF173643	and AF088884.	AI809182, and AI014526.		
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octwice in	601		1 - 330	15 - 304	AA496105, AL038451, AA020916, AA214222, AL038833, AW239553, AL038903, AL036026, W94506 H11258 H10187 T00424 AW153325 AA08409, AA85409
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					A1002404. AA281162. N33973. W67690. A A056138. A A05667. A A22604. A A22604.
					AA252722, AA308905, H37946, AA159207, AA337502, H15180, N35548, T78050, A7114130
					H45908, AL036764, AL038918, AA486190, N99529, AA176166, T29922, A A172728
				~	A1929392, AA993699, T32147, W92551, AA314753, W70343, A1028519, W57361 D12450
					R17656, D30841, D56168, AA018894, AW375983, AA318870, R57052, AA082019, AA018606
					AA401854, W94711, H82178, AB014888, AB015799, AF075601, AF060703, AB015708
					AF080569, AB028854, and AF035962.
HTEGN63	1060	520037	1 - 196	15 - 210	AB007131, AP001052, and AP001051.
HTEG005	1061	932583	1 - 1086	15 - 1100	AA059465, AA059211, AA731209, AA236961, T86500, T87461, AI 024498, and M25862
HTEGQ21	1062	923059	1-419	15 - 433	AA382826, AA382492, AI917341, AI967930, AI990328, AI041198, AW135194, AI936466,
					A1990195, A1336861, A1825657, AA609860, A1652939, A1950262, and A1968690.
HTEGQ74	1063	573865	1 - 358	15 - 372	
HTEGR56	1064	959871	1 - 186	15 - 200	
HTEGR88	1065	871611	1 - 405	15 - 419	AL133660,
HTEGS16	1066	527914	1 - 340	15 - 354	
HTEGS34	1067	458520	1 - 391	15 - 405	D80168 D59677 C14298 D51079 D59695 D57201 D90040 A32250730 D55503
					C14227, D80290, C14389, AW377669, AW352172, T11417, D8028, PX0064, D58246
					D59889, D52059, D45273, D80014, D80391, AW377661, D59787, D80196, D57482, T03048
					C16955, AI557751, D59484, AI535686, Z33452. C06015, AI557774 T07974 C04687
					AA514184, H67854, H67866, AI525216, AI525228, D51053. AI535961, D80251, N66479
					AI525969, AI525238, AI525222, AI525227, AB010386, AR016808, U37689, 181198, X64588,
10000	9,00		,		182446, AB019242, and A47134.
TITE COSTS	1000	500005	1 - 395	15 - 409	
H1EG129	1069	870638	1 - 463	15 - 477	AA610046, AA725767, AA609763, AA694482, AI674115, and AI222344
HTEGT33	1070	716783	1 - 505	15 - 519	AA459933, and AA460208.
HTEGU13	1071	520041	1 - 380	15 - 394	AA725598, AA437008, AA758847, and AA383617.
HTEGU32	1072	524053	1 - 492	15 - 506	AI208922, AF012358, AC000359, AF176024 and AC000357
HTEGU62	1073	573885	1 - 307	15-321	
HTEGU93	1074	764831	1 - 721	15 - 735	AL037365, AI968379, AA397716, AI016755, AI340264, AA626104, AA435927, AA506126,
HTEGVOR	1075	050888	1 435	15 430	and All 1990A.
HTECKER	1076	933054	1 401	15 - 439	APU002/15, AP000105, AP000037, and AC002452.
DIEGVOU	10/0	87777	1 - 484	15 - 498	AA210913.

	Т	T	Т	Т	$\neg$	$\top$	т.	Т.	Т	Т	$\neg$					
AI809518, AA725632, AA400546, AW303510, AA621301, AA400438, AI184200, AI016652, AI698674, AA758091, AA75258, AA725799, and AA705799	AF169385, and AF149310.		AA789286, AI339366, AI656082, AA861573, AA416690, AI808240, AA889130, and AI216654.		AL080197, AP000346, and AL022324	AA383326, and AI672505.	298752.	AA436088, A1149899, A1002083, AA411806, AA470059, AA781801, AA416972, AA435988, AA788635, and AA707579			AI018790, AA885492, AI377750, AW340453, and AC007114	AA421403, AA411967, AA412565, AI825585, AW136990, AI962705, AI825455, and AA889516.	AA577770, H53039, AA515742, AI222360, AA837716, AL109628, AC006064, AL022721, AP001052, AC004694, AL109801, AL117258, AL109759, AC004884, AC005476, 295116, AL022159, AC005015, AC003101, AL035086, 299943, U91323, U91318, AC007773, AC005261, AC002350, AL031289, AC005081, AC005529, U73640, AC005552, AC007040, AL133244, AC006163, AC007285, AC007057, AL121655, AC006324, AR036572, AP000092, AC005829, AL132777, AP0000512, AC000025, AF107257, AC005520, AF107258, AP0000536, AC004814, AC006581, AC010168, AC005790, AL049759, AC005529, AF107258, AP000501, AL121652, AP000510, AL031584, AC009516, AC006441, AC005387, AP000501, AL121652, AP000510, AL034548, AF196969, AC0064991, AC00490571, AC004906, AC004815, AL031681, AC007617, AF196779, AC004707, AB023050, Z83844, AC002312, Z82190, AC005037, AC004990, AC002565, AC007386, AF134726, AL034649, Z82208, AC0066966, and AC003086.	A1033/40, A1223011, AA3933/4, AF000346, AL022324, and AL080197.	AL137678, and AL109657.	AA446074, AJ224924, and AA868166.
15 - 773	15 - 420	15 - 540	15 - 558	15 - 452	15 - 314	15 - 350	15 - 327	15 - 737	15 - 624	15 - 346	15 - 565	15 - 691	15 - 514	15 - 333	15 - 438	15 - 696
1 - 759	1 - 406	1 - 526	1 - 544	1 - 438	1 - 300	1 - 336	1 - 313	1 - 723	1-610	1 - 332	1 - 551	1 - 677	1 - 520	1-319	1 - 424	1 - 682
870240	573880	794350	783829	917214	573849	870707	526704	973071	866596	573882	795264	784926	790342	667224	836999	933624
1077	1078	1079	1080	1081	1082	1083	1084	1085	1086	1087	1088	1089	1091	1092	$\vdash$	1094
HTEGV84	HTEGW41	HTEGW94	HTEGX74	HTEGY01	HTEGY85	HTEHB07	HTEHC20	нтенс47	HTEHC60	HTEHC78	HTEHE60	нтене67	HTEHE91	HTEHF13	HTEHF66	HTEHG44

HTEHI54         1097         533960         1 . 338         15 . 332         R19058, Z44007, F06961, and FI           HTEHI62         1098         922559         1 . 310         15 . 404         AI202243, AA687318, and AII8           HTEHI03         1098         870629         1 . 317         15 . 331         AI202243, AA687318, and AII8           HTEHI04         1100         587062         1 . 317         15 . 331         AA926746           HTEHK0         1101         771432         1 . 430         15 . 428         AL042716, AI634081, AI656008           HTEHCS         1103         573866         1 . 414         15 . 428         AL042716, AI634081, AI656008           HTEHCS         1103         573851         1 . 664         15 . 433         AA393345, AI018421, AI018412           HTEHPO         1100         577851         1 - 664         15 . 433         AA429653, and AL137385.           HTEHPO         1101         573853         1 . 439         15 . 233         AA429653, and AL137385.           HTEHPO         1101         573851         1 . 260         15 . 239         AA429653, and AL137385.           HTEHRS         1111         573813         1 . 346         15 . 336         AA625735, and AL137385.           HTEHRS	and ACOLLOSS.
1098         922559         1 - 390         15 - 404           1099         870629         1 - 317         15 - 331           1100         530749         1 - 235         15 - 249           1101         660875         1 - 317         15 - 331           1102         771432         1 - 430         15 - 444           1103         573866         1 - 414         15 - 428           1104         573859         1 - 390         15 - 438           1105         787521         1 - 664         15 - 678           1106         920625         1 - 429         15 - 333           1107         967443         1 - 379         15 - 333           1108         573853         1 - 379         15 - 333           1109         573853         1 - 425         15 - 339           1110         573841         1 - 250         15 - 339           1111         573841         1 - 250         15 - 359           1111         573813         1 - 345         15 - 359           1111         573813         1 - 345         15 - 359           1114         573813         1 - 345         15 - 368           1115         786378         1 - 3	R19058, Z44007, F06961, and F05366.
1099       870029       1-317       15-331         1100       530749       1-235       15-249         1101       660875       1-317       15-331         1102       771432       1-430       15-444         1103       573866       1-414       15-428         1104       573859       1-390       15-404         1105       787521       1-664       15-678         1106       220625       1-429       15-439         1107       967443       1-379       15-333         1108       531505       1-219       15-439         1110       751866       1-425       15-439         1110       753853       1-379       15-339         1110       751866       1-425       15-339         1111       573853       1-345       15-339         1111       573851       1-345       15-339         1111       573851       1-345       15-359         1111       786378       1-345       15-359         1116       870083       1-377       15-391         1117       924832       1-454       15-36         1120       78652 <td< td=""><td>AI202243, AA687318, and AI184808.</td></td<>	AI202243, AA687318, and AI184808.
1102   660875   1-317   15-331   1102   771432   1-430   15-444   1103   573866   1-414   15-428   1104   573859   1-390   15-404   1105   787521   1-664   15-678   1106   920625   1-429   15-433   1107   967443   1-319   15-233   1108   573853   1-439   15-439   15-439   15-338   1110   573841   1-260   15-274   1113   529280   1-324   15-359   1114   573813   1-345   15-359   1115   573841   1-260   15-274   115-360   117   920610   1-356   15-370   1118   78552   1-454   15-453   1120   760552   1-454   15-453   1120   760552   1-440   15-454   1121   924826   1-502   15-516   1121   924826   1-502   15-516   1122   772643   1-440   15-214   1123   668553   1-200   15-214   1124   527167   1-442   15-456   1125   859130   1-442   15-456   1-445   15-456   1-445   1-4	
1102         771432         1-430         15-444           1103         573866         1-414         15-428           1104         573859         1-390         15-404           1105         787521         1-664         15-678           1106         920625         1-429         15-443           1107         967443         1-379         15-393           1108         531505         1-219         15-439           1109         573853         1-425         15-439           1110         573841         1-260         15-439           1111         573841         1-260         15-368           1111         573841         1-360         15-374           1113         529280         1-324         15-368           1114         573813         1-345         15-368           1115         786378         1-360         15-370           1116         870083         1-377         15-391           1118         785652         1-454         15-468           1119         924832         1-439         15-468           1120         760552         1-286         15-300           1121 <td></td>	
1103         573866         1-414         15-428           1104         573859         1-390         15-404           1105         787521         1-664         15-678           1106         920625         1-429         15-393           1107         967443         1-379         15-393           1108         531505         1-219         15-333           1109         573853         1-429         15-333           1110         751866         1-425         15-333           1111         573841         1-260         15-234           1111         573841         1-260         15-359           1111         573813         1-345         15-359           1114         573813         1-345         15-359           1116         870083         1-377         15-359           1116         870083         1-377         15-368           1117         920610         1-356         15-368           1118         785652         1-454         15-468           1120         760552         1-286         15-360           1121         924826         1-502         15-454           1121 <td></td>	
1104         573859         1-390         15-404           1105         787521         1-664         15-678           1106         920625         1-429         15-443           1107         967443         1-379         15-393           1108         531505         1-219         15-233           1109         573853         1-439         15-233           1110         751866         1-425         15-453           1111         573830         1-354         15-368           1112         573841         1-260         15-274           1113         529280         1-324         15-359           1114         573813         1-345         15-359           1115         786378         1-360         15-359           1116         870083         1-377         15-359           1116         870083         1-377         15-350           1118         785652         1-454         15-368           1120         760552         1-454         15-468           1121         924826         1-502         15-454           1121         924826         1-502         15-454           1123 <td></td>	
1105         787521         1 - 664         15 - 678           1106         920625         1 - 429         15 - 443           1107         967443         1 - 379         15 - 393           1108         531505         1 - 219         15 - 233           1109         573853         1 - 439         15 - 453           1110         751866         1 - 425         15 - 439           1111         573830         1 - 354         15 - 358           1112         573841         1 - 260         15 - 274           1113         529280         1 - 324         15 - 359           1114         573813         1 - 345         15 - 359           1115         786378         1 - 345         15 - 359           1116         870083         1 - 345         15 - 376           1118         785652         1 - 454         15 - 36           1119         924832         1 - 454         15 - 36           1120         760552         1 - 454         15 - 516           1121         924826         1 - 502         15 - 516           1121         924826         1 - 502         15 - 454           1123         668553         1 - 440	
1106         920625         1-429         15-443           1107         967443         1-379         15-393           1108         531505         1-219         15-233           1109         573853         1-439         15-453           1110         751866         1-425         15-439           1111         573830         1-354         15-368           1112         573841         1-260         15-274           1113         573841         1-260         15-274           1113         573841         1-36         15-359           1114         573813         1-345         15-359           1116         870083         1-377         15-391           1116         870083         1-377         15-391           1117         920610         1-356         15-301           1118         785622         1-454         15-468           1120         760522         1-454         15-454           1121         924826         1-502         15-516           1121         924826         1-502         15-454           1123         668553         1-240         15-454           1124 <td>AL042716, AI634081, AI656008, AI383457, AA298264, AW274940, AW183456, AI824911, H48934, and AI015007.</td>	AL042716, AI634081, AI656008, AI383457, AA298264, AW274940, AW183456, AI824911, H48934, and AI015007.
1107         967443         1-379         15-393           1108         531505         1-219         15-233           1109         573853         1-499         15-439           1110         751866         1-425         15-439           1111         573830         1-354         15-368           1112         573841         1-260         15-274           1113         529280         1-324         15-376           1113         529280         1-345         15-359           1114         573813         1-345         15-376           1116         870083         1-377         15-391           1117         920610         1-356         15-370           1118         785622         1-454         15-36           1119         924832         1-454         15-468           1120         760552         1-286         15-300           1121         924826         1-502         15-516           1122         772643         1-440         15-454           1123         668553         1-200         15-214           1124         527167         1-447         15-456	
1108         531505         1-219         15-233           1109         573853         1-439         15-453           1110         751866         1-425         15-439           1111         573830         1-354         15-368           1112         573841         1-260         15-274           1113         529280         1-324         15-338           1114         573813         1-345         15-359           1115         786378         1-362         15-376           1116         870083         1-377         15-391           1117         920610         1-356         15-370           1118         785622         1-454         15-468           1119         924832         1-454         15-468           1120         760552         1-286         15-468           1121         924826         1-502         15-454           1122         772643         1-440         15-454           1123         668553         1-200         15-454           1124         527167         1-447         15-454	AA393345, AI018421, AI018412, and AI621296.
1109         573853         1-439         15-453           1110         751866         1-425         15-439           1111         573830         1-354         15-368           1112         573841         1-260         15-274           1113         529280         1-324         15-338           1114         573813         1-345         15-359           1115         786378         1-362         15-376           1116         870083         1-377         15-391           1117         920610         1-356         15-376           1118         785652         1-454         15-468           1119         924832         1-439         15-453           1120         760552         1-286         15-300           1121         924826         1-502         15-454           1122         772643         1-440         15-454           1123         668553         1-200         15-214           1124         527167         1-477         15-456	
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1111         573830         1 - 354         15 - 368           1112         573841         1 - 260         15 - 274           1113         529280         1 - 324         15 - 338           1114         573813         1 - 345         15 - 359           1115         786378         1 - 362         15 - 376           1116         870083         1 - 377         15 - 391           1117         920610         1 - 356         15 - 370           1118         785652         1 - 454         15 - 468           1120         760552         1 - 286         15 - 300           1121         924836         1 - 396         15 - 356           1121         924826         1 - 502         15 - 516           1121         924826         1 - 502         15 - 516           1122         772643         1 - 440         15 - 454           1123         668553         1 - 200         15 - 214           1124         527167         1 - 477         15 - 456	and AL137385.
1112         573841         1 - 260         15 - 274           1113         529280         1 - 324         15 - 338           1114         573813         1 - 345         15 - 359           1115         786378         1 - 362         15 - 376           1116         870083         1 - 377         15 - 391           1117         920610         1 - 356         15 - 370           1118         785652         1 - 454         15 - 468           1120         760552         1 - 286         15 - 300           1121         924832         1 - 286         15 - 30           1121         924826         1 - 502         15 - 516           1122         772643         1 - 440         15 - 454           1123         668553         1 - 200         15 - 214           1124         527167         1 - 477         15 - 456           1125         859130         1 - 442         15 - 456	
1113         529280         1-324         15-338           1114         573813         1-345         15-359           1115         786378         1-362         15-376           1116         870083         1-377         15-391           1117         920610         1-356         15-370           1118         785652         1-454         15-468           1120         760552         1-286         15-300           1121         924826         1-502         15-516           1121         924826         1-502         15-516           1123         668553         1-440         15-214           1124         527167         1-447         15-456           1125         889130         1-442         15-456	and AW275130.
1114         573813         1-345         15-359           1115         786378         1-362         15-376           1116         870083         1-377         15-391           1117         920610         1-356         15-370           1118         785652         1-454         15-468           1120         785652         1-439         15-463           1121         924826         1-502         15-516           1121         924826         1-502         15-516           1122         772643         1-440         15-454           1123         668553         1-200         15-214           1124         527167         1-447         15-456           1125         8859130         1-442         15-456	
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1116         870083         1-377         15-391           1117         920610         1-356         15-370           1118         785652         1-454         15-468           1119         924832         1-439         15-453           1120         760552         1-286         15-300           1121         924826         1-502         15-516           1121         924826         1-440         15-454           1123         668553         1-200         15-214           1124         527167         1-477         15-491           1125         859130         1-442         15-456	A868749.
1117         920610         1 - 356         15 - 370           1118         785652         1 - 454         15 - 468           1119         924832         1 - 439         15 - 453           1120         760552         1 - 286         15 - 300           1121         924826         1 - 502         15 - 516           1122         772643         1 - 440         15 - 454           1123         668553         1 - 200         15 - 214           1124         527167         1 - 447         15 - 491           1125         859130         1 - 442         15 - 456	
1118     785652     1-454     15-468       1119     924832     1-439     15-453       1120     760552     1-286     15-300       1121     924826     1-502     15-516       1122     772643     1-440     15-454       1123     668553     1-200     15-214       1124     527167     1-477     15-491       1125     859130     1-442     15-456	60, and Z62661.
1119     924832     1-439     15-453       1120     760552     1-286     15-300       1121     924826     1-502     15-516       1122     772643     1-440     15-454       1123     668553     1-200     15-214       1124     527167     1-477     15-491       1125     859130     1-442     15-456	
1120         760552         1 - 286         15 - 300           1121         924826         1 - 502         15 - 516           1122         772643         1 - 440         15 - 454           1123         668553         1 - 200         15 - 214           1124         527167         1 - 477         15 - 491           1125         859130         1 - 442         15 - 456	
1121     924826     1 - 502     15 - 516       1122     772643     1 - 440     15 - 454       1123     668553     1 - 200     15 - 214       1124     527167     1 - 477     15 - 491       1125     859130     1 - 442     15 - 456	H99838, AL037447, H98172, R99332, and N73909.
1122     772643     1 - 440     15 - 454       1123     668553     1 - 200     15 - 214       1124     527167     1 - 477     15 - 491       1125     859130     1 - 442     15 - 456	AI198906, AI743542, AI807563, AI392615, AI813744, AI150517, and AI150519.
1123     668553     1 - 200     15 - 214       1124     527167     1 - 477     15 - 491       1125     859130     1 - 442     15 - 456	AI699984, AA470157, AI018717, AI917728, AA398746, AA393334, AI216704, AA868127,
1124         527167         1 - 477         15 - 491           1125         859130         1 - 442         15 - 456	
1125 859130 1 - 442 15 - 456	
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663096		958355	573828	699470	573826	520113	712520	958241	772402	967431	530454	789121	953803	523681	520045	760551	753210	+	920622	653244	573803	941155	. 253865	765794	928058		573775	779163	870652	922027
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HTEIB14		HIEIF40	HTEIF68	HTEIG32	HTEIH70	HTEIJ17	HTEIJ41	HTEIJ73	HTEIJ77	HTEIK11	HTEIK70	HTEIK90	HTEIL07	HTEIL48	HTEIL70	HTEIL71	HTEINER	HTEIN95	HTEI002	HTEI012	HTEI028	HTEIP88	HTEIP92	HTEIQ74	HTERR33		HTEIS65	HTEIU75	HTEIU92	HTEIV54

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HTEIV86	1156	784657	1 - 476	15-490	AA884237, and Z66028.
HTEIW27	1157	829698	1 - 790	15 - 804	AL040266, AA045127, H71355, AA070703, AA036715, AA325559, AA043642, AA196645, H94227, AA305440, AA383234, H61672, H06121, R60099, AL042836, AI016643, AW410572, AL042837, and AI018804.
HTEIW37	1158	573891	1 - 340	15 - 354	
HTEIX28	1159	836011	1 - 725	15-739	AA878363, AL040461, AI806762, AL040944, N48708, AA961620, AI015474, AI122718,
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HTEIX85	1160	864251	1 - 364	15-378	AI143096, AA476476, AF112968, and AF133914.
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HTEIY69	1162	577783	1 - 342	15-356	AA860220, AA373213, AA095300, AA294896, AA056395, AW369291, AA081316, AA081068,
					AA258633, AA491648, T78543, AI565548, T68394, D81309, AA303509, C02623, AA552624,
HTEIY80	1163	955242	1 - 640	15 - 654	AI206714, AI962380, AW139167, AI341507, AW197295, AF146793, and AC004673.
HTEIZ76	1164	523764	1-373	15-387	
HTEJB20	1165	528015	1 - 336	15 - 350	AW119138, AA508616, and AC000386.
HTEJB25	1166	530590	1 - 364	15-378	AI804160, AI287878, AA400787, AI003207, AF176315, AF042089, AC007040, AC000385, and AC004967.
HTEJB81	1167	870644	1 - 326	15 - 340	AC005230, and AL031230.
HTEJC28	1168	573774	1 - 292	15 - 306	
HTEJC95	1169	772989	1-412	15 - 426	
HTEJE15	1170	908360	1-577	15 - 591	AI217144, AA399611, AA398976, AI025074, AA758412, AW449170, AI953070, AI337133, AI654417, AA608877, AI969018, AA400066, AA401568, AL137462, and S75275.
HTEJES0	1171	520049	1-410	15 - 424	AA383469.
HTEJF45	1172	942476	1 - 704	15 - 718	AA927155, AI989936, AI870479, AW196902, and AW137017.
HTEJG24	1173	526278	1 - 432	15 - 446	
HTEJJ43	1174	774243	1 - 505	15 - 519	
HTEJL21	1175	573742	1 - 460	15 - 474	AA913820, AW138390, W37338, A1139797, AW135343, AA776708, AA621016, AW274952, A1623224, A1125250, AA778537, A1208106, A1637631, AW341652, AA776715, A1204215, AA609761, A1671266, A1023591, A1950399, AA758819, AW104292, A1188024, AW058598.

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AA460183, AI969065, W37337, and AA824405.	AL042395, AA504349, AI693474, AI125391, AL041671 AW168041 AA838043 AT0000115	AI864457, AI149664, AI738586, AL041569, AW294188, AI805280, AA579771, AW273185	AI653680, AW197733, AI138789, AI699335, AI475427, AA883961, AI203057, AI968077.	AA383594, AA976749, AI648684, AI952360, AI680162, AI590021, AW076093, AW264516	A1073952, A1568870, A1564719, A1623828, AA808060, A1683684, A1866457, A1628292	AW196868, AW075413, AI590686, AI867042, AI922365, AW081255, AI285586, AI740175	AI610293, AW103878, AI915576, AW403717, AI475455, AI811860, AI282903, A1539808	AI873644, AI174394, AI469811, AI831140, AI872910, AI690585, AI519829, AI863101	AI613270, AI625464, AI281660, AI870187, AI886022, AI769862, AI624303, AI002121,	AI680498, AI934259, AI610114, AW193026, AI 171770, AI789337, AW75657, A1364709	AI383919, AW168723, AI922901, AI636719, AW073697 AIR63371 AI770055 AI633773	AI624543, AI610645, AI702433. AI611743. AI690312. AI.039776. AI689420. AI.045400	AW080992, AI687065, AI432040, AL048656, AI819326, AW238730, AI445976, AI744756	AA572758, AL045163, AI627880, AI866741, AI805385, AI612771, AI 119791, AW070159	AI343059, AI619716, AI828731, AI612759, AW089179, AW151729, AI696819, AI870192	AIS67351, AI349933, AI934011, AI280661, AI699011, AI537617, AI919345, AI251830	AW088899, AI366549, AI539153, AW088144, AL036214, AI866608, AI859464, AI866585	AI499986, AW149236, AW083804, AI862144, AW170734, AI696626, AL040241, AI554821	AI589993, AW059713, AI921082, AL038445, AW168425, AI345111, AI446373, AI358701.	AL036638, AI537677, AI621179, AI433157, AL041150, AI537837, AI159837, AI874351,	AL038882, AI520785, AI609059, AI344817, AI539771, AI798258, AI922577, AI471361,	AI500659, AI288285, AI889168, AI344935, AI866573, AW068845, AW103228, AL045620.	AI476109, AI815232, AI801325, AI500523, AI573060, AW302965, AA640779, AI345608,	AI582932, AI284517, AA613907, AI500706, AI445237, AI491776, AI758613, AW151138,	AL042628, AI521560, AI889189, AI500662, AI284509, AI439452, AI857724, AW148320,	AI633493, AW169653, AI434256, AI344785, AI249962, AL041772, AI609677, AI888661,	AI811344, AI284513, AI620284, AI888118, AI349614, AI872051, AI589273, AI866510,	AL569583, AW302992, AI801112, AW088903, AI440252, AI800152, AI963068, AI569632,	AI274769, AI348854, AL036664, AW023590, AI608676, AI345471, AW088134, AA579232.	AA494167, AW075084, AI468872, AA420722, AI537307, AL120853, AL040243, AI251205,	A1924971, AI287489, AI698401, AI524607, AI683714, AL043632, AL043326, AI538342.	N71180, A1433976, AC003688, AF096834, AF073955, AF073954, AL117585, S68736, A08916,	A08910, AR000496, U39656, A08909, I48978, I89947, A08913, U72620, I89931, I49625,	AL049382, AF090896, AL080060, 126207, AL137556, AL137283, AF113676, AL137538,
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HTEJP66	1181	916481	1 - 697	15 - 711	AW402599, AA402458, N28458, W04863, AA683291, C17218, AA452695, AA321934.
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HTEJT74	1184	676254	1 - 438	15 - 452	AA393248, AA393292, AI796754, AA293815, AA459841, AI075905, AW137492, AI652522, AI217933, AI150346, AI694956, AA399502, AA398164, AI024099, AA719008, AA629029,
HTEJU30	1185	573823	1 - 304	15-318	AA601041, AA402465, AA455022, K24468, K66361, AA688372, AF081250, and AF081249. AC0000093
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HTEJX78	1187	806395	1-411	15 - 425	AA496111, AW138142, AA306268, AA417106, AA382596, AI027705, AA383788, AI824924,
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HTEIV27	1180	021066	1 220	15 - 440	A1695191.
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UTEVC13	1131	25035	1 - 369	15 - 403	AWU8/802.
HIENCIZ	7611	c/6c18	1 - 345	15 - 359	A1539455, A1218279, A1348415, AW408773, AW340548, A1368160, AA894774, AA937067,
HTEKD04	1193	519938	1-418	15-432	
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HIENER	11.74	2/4044	1 - 133	13 - 749	AL1091081, AC009405, AC005683, AJ239321, AC007253, AL009173, AL030995, Z99572, and AL109853.
HTEKE46	1195	870084	1 - 1112	15 - 1126	AI125483, W77994, AI161017, W73951, AI250771, AA777158, W94063, AA912611, AA339877, AI265865, and AA339786
HTEKE80	1196	790381	1 - 523	15 - 537	
HTEKF04	1197	774260	1 - 732	15 - 746	AA609512, AW074860, AW119172, AA626238, AA759162, AA609090, AA421396, AW070485, AA421292, AW303549, and AC007000
HTEKF24	1198	573750	1 - 412	15 - 426	AF001846.
HTEKF35	1199	573749	1 - 253	15 - 267	
HTEKF68	1200	772997	1 - 567	15 - 581	AW263561, AW183891, AI005584, AI216442, AA983878, AA815385, AA868890, and
UTEVIO	1201	261210	1 410	30,	A1004495.
HIENOI	1071	21/1/0	1-410	15 - 430	
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HTEKM14	1204	745257	1-312	15 - 326	
HTEK049	1205	723148	1 - 383	15 - 397	AA699599, AI275162, N27054, R09201, and AC006211.

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1 - 314	1 - 555	1 - 412	1 - 414	1 - 1063	1 - 333	1 - 495	1 - 426	1 - 490	1 - 286	1 - 304	1 - 304	1 - 407	1 - 1005	1-510	1 - 495	1 - 601	1 - 442	1 - 441	1 - 251	1 - 658	1 - 575	1 - 654	1 - 376	1 - 453	1 - 227	1 - 646
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1206	1207	1208	1209	1210	1211	1212	1213	1214	1215	1216	1217	1218	1710	1220	1221	1222	1223	_		1226	1227	1228	1229	1230	$\neg$	1232
HTEKQ26	нтек (985	HTEKR75	HTEKS15	HTEKS20	HTEKS21	HTEKS76	HTEKX06	HTEKX08	HTEKX28	HTEKX70	HTEKZ50	HTEL A 50	HTEI D47	HTELD82	HTELE10	HTELE41	HTELG47	HTELG57	HTELG80	HTELH44	HTEL103	HTELI51	HTELJ89	HTELK14	HTELK50	HTELK68

		AA913156, AI221124, AA305153, and AF106564.	AI591200, AA102066, AI867662, AW088720, and D26018	AL031597.	AIS40890, AIS57426, AIS57082, AIS41027, AIS47225, and AIS41056.	AL078613.		R80089, X85707, and X85708.	AA310475, AI536833, AA319470, AA278518, AA319408, W20004, AI611260, AA418173, A1968286 AW18225, AA315267 AA401655, AW170378, and A104085	AI125340, AI125684, AI377949, AA884214, AI126470, AI218351, AI243952, AA723933.	AI240603, AI143979, and AI187742.	AA652491, and AF152924.	AI827560, AI336053, AA873745, AA451732, AI436724, AA923591, AA055247, AW189536,	AA747873, and Z40977.	AA746627, AA398848, AA435892, AI208905, AI024568, AA861337, AA861875, and AA910621.	AL033517.	AI799028, AW263660, AA861674, and AA993711		AI198878, AI190586, AI018804, AL042837, AI208256, AA725583, AI016643, AA833661	AA626323, AA993365, AI018351, AA718913, AA725636, AA992718, AI183840, AA403023,	AI911045, R60037, AA398422, AW410573, AA749431, AI128961, AI077415, AI198777,	A1439996, A1934676, A1199096, AA682387, H92998, A1200368, AA778651, AA045098,	AW157530, AW250790, AA587915, AW188549, AI819989, AI951978, AW007464, AI951992,	AI376410, AI677931, AA778720, AI364379, AA584288, AW162769, AI040155, AA150015,	AI187131, AA977318, AI373112, AI000432, AI038499, AI076148, AI278114, W94564,	AA513466, AA946608, AI279549, AI758476, AW103741, AA836837, AI700221, AI253749,	A1913907, AA057355, A1038357, A1758826, H71311, AW004637, AW273537, AA186980,	A1885648, AA824341, W70033, T35014, AI262733, AI693026, AA196549, AI868298,	AI090830, T16464, AL042836, AI887548, AW025276, A1139138, and AA150080.	AC007746.	AI272244, AA382531, AI809639, U35371, and X99043.	AW117507, AW105238, AW105158, AA969617, AI692859, AA934716, AA383047 and
15 - 529	15 - 649	15 - 954	15 - 302	15 - 434	15 - 392	15 - 528	15 - 263	15 - 578	15 - 463	15 - 463		15 - 451	15 - 461		15 - 713	15 - 381	15 - 471	15 - 270	15 - 449											15 - 448	15 - 1100	15 - 782
1-515	1-635	1 - 940	1 - 288	1 - 420	1 - 378	1 - 514	1 - 249	1 - 564	1 - 449	1-449		1 - 437	1 - 447		1 - 699	1-367	1-457	1 - 256	1 - 435											1 - 434	1 - 1086	1 - 768
783824	952267	952269	786268	926910	931120	908192	934344	921621	922634	761768		826531	761598		780619	915339	934302	963576	796832											870615	910946	952241
1233	1234	1235	1236	1237	1238	1239	1240	1241	1242	1243		1244	1245		1246	1247	1248	1249	1250											1221	1252	1253
HTELL48	HTELL51	HTELL90	HTELM89	HTELO20	HTELO51	HTEL073	HTEL093	HTELP27	HTELQ41	HTELQ87		HTELR90	HTELT72		HTELT83	HTELU01	HTELV06	HTELV10	HTELV26											HIELV45	HTELV86	HTELW29

AI917691.	AA393684, AA813816, and AI700752.	AI220445.					AI954673, AI220421, AA813119, AA382989, AI024406, AF113526, AB023063, and AF113510	ACMAGON				AA778498, AI337034, AA609166, AA625857, AI201263, AA437287, AI678062 A1961118	AI203907, AI917789, AA626247, AA927799, AI187708, AA442366, AW294301, and AL050341.	AI813375.	M78994, R86687, T08961, AW402241, R46318, AA349761, AA350295, AA354235, H15340	AI909793, D31764, and AF037332.	AA625914, AA416795, and AC005858.	AI026681, AA609997, AA382092, AA789295, and T12649		AI142370.	H59039.		AA759198, and AA968427.				AA804990.	AL049761.	AA933702 AL036538 AA978649 AA303550 AWINASS AA07777 AA602615 AA602606	AI351083, AA406036, AI004273, AI217923, AA923027, AA435495, AI128197, AA496058, AI187946, AI075847 A 8855071 A 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	AW003084, AA574346, AW188065, AI657112, W37979, AW162204, W37760, AW172598
	15 - 500	15 - 359	15 - 230	15 - 451	15 - 549	15 - 465	15 - 1498	15 - 144	15-416	15 - 547	15 - 308	15 - 384		15 - 461	15-310		15 - 687	15 - 444	15 - 508	15 - 564	15 - 572	15 - 361	15 - 883	15 - 246	15 - 325	15 - 421	15 - 499	15 - 362	15 - 788		15 - 1126
	1 - 486	1 - 345	1 - 216	1 - 437	1 - 535	1 - 451	1 - 1484	1 - 130	1 - 402	1 - 533	1 - 294	1 - 370		1 - 447	1 - 296		1 - 673	1 - 430	1 - 494	1 - 550	1 - 558	1 - 347	1 - 869	1 - 232	1 - 311	1 - 407	1 - 485	1 - 348	1 - 774		1-1112
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	1254	1255	1256	1257	1258	1259	1260	1261	1262	1263	1264	1265		9971	1267		1268	1269	1270	1271	1272	1273	1274	$\dashv$	1276	1277	1278	1279	1280		1281
	HTELW62	HTELX52	HTELX72	HTELY64	HTELZ07	HTELZ89	HTEMA54	HTEMB26	HTEMB28	HTEMB34	HTEMB72	HTEMB83		HTEMC18	HTEMC75		HTEMD10	HTEMD73	HTEMF08	HTEMJ34	HTEM154	HTEMK03	HTEMM80	HTEMN08	HTEMN95	HTEM014	HTEMO85	HTEMP48	HTEMP49		HTEMR65

AI655693, AA283822, AI937864, AA454174, AI016572, AW044162, AW162368, AI420414, AI804706, and AI567345	AW082687, AA774543, AW195592, AW274057, AA460327, AA382893, AI126206, AI198578, AA682221, AW183102, and A 4911000	AA045732, AA412195, T70810, T85978, H76344, A A 202872, A 7242522	A1016782. A1149777. A A 4 4 4 8 0 1 1 A 4 4 4 8 1 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	AW003548, AA757091, AW014801, AA813307, AA437700, AD000204	W90717, and W90708.	AP000470.		AL048534, AA403281, N78348, and AI 031255		AL080132, AC011594, AC006238, R38805, R49132, R49132, H06801, N66174, N08607	AA043641, AA146965, AA147010, AA259116, AA259155, AA534491, AA570283, AA687135	AA766643, AA910635, AA948152, AA401719, AA609258, AA626320, AA644562, AA680291.	AA757030, AA758747, AA888971, AI023819, AI032507, AI088947, AI274536, AI345946,	A1431770, A1192387, A1214901, and A1217881.		AW195712, D44825, A1124542, and AB032984.		A1473748, A1798241, A A 279454, A I 138273, and A WI 140414	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		AA393073, AI139819, AA860114, AA412161 and AA868102	A1970129, AW237169, A1621267, A1653036, A1797400, A1797775, AW182022, A1621267	AI970364, AI191623, AL036577, AW188292, AI341330, AI655836, AA918201, A1202082	AI825213, AI824962, AI990770, AA890172, AI982569. AI918790. 41205504. AI611043.	AI969360, AW293674, AI203082, AI828842, AI634070, AI962396, AA757981, A1917847	AI867911, AI824830, AA903616, AI968361, AA781952, AI 034678, and A 6450330	AI240133, and AF032967.	AF012383, AI307797, AW270088, and 1186074		AL042436, AL042437, AIG74705, AA400083, AW241753, AA401372, AI218464, AA953011,	
	15 - 400	15-355	15 - 650	15 - 644	15 - 349	15 - 450	15 - 539	15 - 233	15 - 377	15 - 734			•	15 400	024 - 21	15 - 574	15 - 757	15 - 347	15 - 309	15 - 105	15 - 615	15 - 650					15 - 1028	15 - 445	15 - 566	15 - 913	15 - 1468
	1 - 386	1 - 341	1 - 636	1 - 630	1 - 335	1 - 436	1 - 525	1 - 219	1 - 363	1 - 720				1 - 476	2/2	1 - 560	1 - 743	1 - 333	1 - 295	1 - 91	1 - 601	1 - 636					1 - 1014	1 - 431	1 - 552	668 - 1	1 - 1454
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	1282	1283	1284	1285	1286	1287	1288	1289	1290	1291				1292	1202	1293	1294	1295	1296	1297	1298	1299					1300	┪	-	1303	1304
	HTEMS10	HTEMS48	HTEMT06	HTEMT89	HTEMU17	HTEMU54	HTEMX92	HTEMY30	HTEMZ04	HTENA22				HTENB03	LTENICO	HIENC22	HIENF08	HTENF95	HTENG66	HTENG93	HTENH86	HTENIS8					HTENJ28	HTENJ76	HTENK06	HTENK69	HTEN012

HTENO50	1305	969213	1 - 635	15 - 649	1 21
HTENP54	1306	787535	1 - 494	15 - 508	AA496169, and AC009411.
HTENP80	1307	775387	1 - 482	15 - 496	AL035453.
HTENQ05	1308	928244	1 - 641	15 - 655	AA393064.
HTENR10	1309	963530	1 - 575	15 - 589	
HTENR74	1310	764828	1 - 444	15 - 458	AI823791, and AF069682.
HTENR93	1311	920834	1 - 875	15 - 889	AI381463, AA634395, AA406053, AA405219, AA383176, and AF121781.
HTENS22	1312	785996	1 - 532	15 - 546	H83100, AL044519, and AL137391.
HTENS43	1313	784936	1 - 1079	15 - 1093	AI971582, H58143, AI499833, AI393537, and AA973074.
HTENS91	1314	870515	1 - 720	15 - 734	AA225153, AA629286, AA225136, AI272649, AA909816, AA070899, AI866377, AA229443,
,					R67086, AA084212, AW243884, H59093, AA158549, AC002086, AL133304, AC000004,
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					AC007226, AL049694, AC004143, AL022476, Z93244, Z68284, AP000359, AC005015,
					AL034429, AC000394, AC006120, AC003029, AL031589, AC004782, and AL035072.
HTENV57	1315	944416	1 - 605	15-619	
HTENW53	1316	_	1 - 806	15 - 820	AA429691, AA429515, AC007114, Z61140, and AC004156.
HTENX77	1317	771409	1 - 521	15 - 535	AA781188, AA460513, AA860910, AA781845, AI027285, AI208471, AA889700, N73782,
					H08088, R38703, F03385, A1830535, A1474644, R41444, AA459870, A1023552, and
	1	202000		0.6	AA421061.
HTENY21	1318	870587	1 - 705	15-719	A1/43533, A1424822, AW082413, and A1915340.
HTENY35	1319	884043	1 - 1011	15-1025	AJ223811, X85630, T36006, AA382232, Z21393, AA383107, N78092, T36070, T36050,
					Z21341, Z21392, AA459806, Z21315, AF012377, Z21111, AI827647, AW340665, AA280976,
					Z21340, T85719, AL043525, AL043526, R82847, AC006208, and AL137671.
HTENZ16	1320	917185	1 - 962	15 - 976	AI018671, AI807205, AI468026, AI797263, AI025828, AW194247, AI889876, AA843455,
					A1884356, A1198561, A1032059, A1126485, A1889886, A1239452, AA992969, AA780875,
					AW303976, AI216470, AA683361, AI569512, AI472962, AI885458, AW055338, AW242149,
					AI911290, AI222107, AI538002, AA912612, AW183126, H79395, AA884115, AI149911,
					AW189703, AI220396, AI203939, AA936147, AIS60168, AI219573, AW243836, AA906293,
					AI252658, N26330, N26296, AI886564, AW085495, AA927058, and AL133596.
HTENZ33	1321	870591	1 - 616	15 - 630	AA383398.
HTENZ72	1322	773024	1 - 564	15 - 578	AI632084, AI221893, AA383392, AA759214, AW137663, AI269516, and AA923222.
HTEOA90	1323	787516	1 - 489	15 - 503	AA383437,
HTEOD34	1324	812307	1 - 552	15 - 566	AI990671, and AI990110.
HTEOE61	1325	918635	1 - 548	15 - 562	

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15 - 633	15 - 520	15 - 508	15 - 251	15 - 530	15 - 436				15 - 409	15 - 992	15 - 349	15 - 653	15 - 439													_								
1-619	1 - 506	1 - 494	1 - 237	1 - 516	1 - 422				1 - 395	1 - 978	1 - 335	1 - 639	1 - 425									<del></del>						-						
793202	847224	768583	918571	870575	810333				918590	815852	954114	915138	870532																			•		
1326	1327	1328	1329	1330	1331				1332	1333	1334	1335	1336																					1
HTEOF31	HTEOF80	HTEOF85	HTEOF91	HTEOI36	HTEOIS3				HTEOK02	HTEON29	HTEON67	HTEOU45	HTEOV90																					

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	1 - 596	1 - 488	1 - 649	1 - 1054	1 - 589	1-610	1 - 580	1 - 526	1-514			
	918475	870566	969682	958391	872923	772949	782248	767824	883021			
	1337	1338	1339	1340	1341	1342	1343	1344	1345			
	HTEOW02	HTEOW39	HTEOW85	HTEPA08	HTEPA27	HTEPB66	HTEPB84	HTEPC76	HTEPC87			_

		AI283483, AI873282, and AI827738.			3 AI217947, AW237109, AI918745, AI968403, AA934788, and X84603	AI217204, AW183426, and AA759358.	AA397836, AI139919, AW162347, AI223276, AI879324, AI200822, AI150592, AI028601.	AI200868, AI879701, AI138943, AI652314, AI377443, AA868111, AW160551, and AF177398	AI624244, AL120897, AL121756, AC007099, Z99496, AC004584, AC002418, AP000248	AC004386, AL050305, AC002483, AL022315, AL034452, AC004638, AC005899, AC000353	AC004623, Z84476, and U91323.	AI623182, AA776747, AW082325, AW273819. AI539350, AI810085, AI175567, AI721672	AI200770, AI204194, AW263528, AI240146, AA437189, AA738317, AI192035, AA709217,	A A 992316, A A 758401, A A 961979, A 1217262, and 266485.		AA913948, AI633873, AI638029, AI990760, AI806847. AW003193, AI190550, AA431560	AI187284, AI915840, AI286045, AI243468, AA719044, AA448281, AI219847, AW135537,	AA861812, AA861291, AI969788, AA812901, AI187727, AI286137. and AI942348		AW299627, AA917835, AA758010, AI989828, AW103119, and AW241908	(1) The state of t	AA383039.	AA382997, and AA397859.		AA609033, AA293870, AA382673, AW263657, and US1244.	AI979286, AA382595, and AF133424.	AI990882, AA447560, AI201149, AI341615, AW002367, AI651854, AA437021. AI149956	AI140621, AW292211, AA620811, AW196416, AA757082, AA993629, AA932499, N92273,	AA448543, AI458277, AA398159, AW004057, AI918824, AI635506, AA401699, AA994466,	and A1010246.	71142270, AA417363, and Al148003.	•
15 - 169	15 - 407	15 - 644	15 - 718	15 - 503	15 - 1363	15 - 543	15 - 574		15-410			15 - 557			15 - 621	15 - 743			15 - 591	15 - 617	15 - 510	15-510	15 - 389	15 - 141	15 - 604	15 - 770	15 - 570			15 1217	15, 361	
1 - 155	1 - 393	1 - 630	1 - 704	1 - 489	1 - 1349	1 - 529	1 - 560		1 - 396			1 - 543			1 - 607	1 - 729			1 - 577	1 - 603	1 - 496	1 - 496	1 - 375	1 - 127	1 - 590	1 - 756	1 - 556			1 1208	1 - 347	
787499	870509	870637	915134	917406	840028	963433	888470		922941			915198			918579	958354	-		881004	853971	870525	806495	806504	966141	932301	939641	966486			924799	530577	
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HTEPR90	HTEPT25	HTEPT75	HTEPU01	HTEPV02	HTEPX32	HTEPZ10	HTEPZ18		HTEQB03			HTEQD40			HTEQD69	HTEQE87			HTEQG56	HTEQI54	HTEQ114	HTEQJ42	HTEQ081	HTEQP45	HTEQQ82	HTEQR15	HTEQR94			HTEOT63	HTLAB19	

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AF038406.		AI217166, AI184534, AI150079, AI142754, AI697160, AI811701. AI214713. and AW188915		AA418228, AF045454, D63648, and E13935.	AC005258.	AL121757.	AL036680, AA421020, AW151136, R66759, AL037558, AL045421, AA830821, AW149876.	AI571529, AI355008, AI567582, AW089006, AI471361, AW0233338, AW020095, AL041150	AW167924, AI829990, AI345224, AI079736, AL046463, AI311892, AW162194, AI697324	T99953, AW243637, AI921167, AA291456, AI539771, AI873638, AI473451, AI805688	AI888621, AI828574, AW022682, AW239367, AI540606, AI689420, AI336662, AL038575.	AA464646, AW020693, AI890887, AI590423, AI570966, AI307507, AI916419, AI611728.	AI470293, AI929108, AI538850, AI610667, AA572758, AI648567, AW088899, AI805638	AI366549, AI799195, AI866082, AI636719, AI539153, AI620093, AI866608, AI636619	AL120853, AI340603, AI537677, AI611743, AW083804, AI349598, AI582912, AW172723.	AI539800, AI696626, AI349256, AW075207, AI589993, AI866573, AI312152, AI365256	AA579232, AA807088, AI343037, AI345735, AW085786, AW265004, AW075084. AI310925.	AL038564, AI472536, AI312399, AI677797, AW082600, AI349937, AI567944, AI345688.	AI334884, AI307543, AI494201, N71199, AI345251, AW071412, AI307210, AI307708,	N29277, AI312325, AW071395, AL036631, AI538885, AI249946, AI244380, AI340659,	AI589267, AW071377, AW129230, AI802240, AW161579, AI313320, AI955906, AI340644.	AI805769, AI434242, AI313352, AI335363, AI307503, AI539707, AI334930, AI309443,	AI623682, AL039086, AI307736, AW161402, AI307520, AI623736, AI446124, AW084097.	AI349266, AI349787, AI334452, AI340664, AI310592, AI344938, AI312146, AI866786,	AI309431, AI312339, AI340537, AW301300, AI345739, AW161202, AI345674, AI345258,	AIS38764, AI312143, AI307459, AI349637, AA635382, AI273179, N74355, AI312428,	AI499974, AI310927, AL110306, AI311604, AI307578, AA420722, AW162189, AI436429,	AI349955, AW189933, AW075093, AI312432, AL120300, AA580663, AI349269, AI312357,	AI590943, AI358701, AW021588, AI310945, AL040241, AW088903, AW151714, AL036638.	AI636581, AI583445, AW059713, AI648408, AI312237, AI922901, AI446373, AW263716.	AI251830, AI343059, AI917963, AI573026, AI349933, AW193467, AW268261, AW082623,	AI249877, AL047422, AL133741, AA493923, AI345253, AW409775, AL119836, AI345677,	AW167918, AA494167, AW191003, AI633402, AL119791, AW071362, AW021373, AI345608,	N98606, AW191844, A1336513, A1357599, AI433968, AI499581, AA848053, AI554821,	AW264/19, AL046618, Al348895, Al345347, AW269097, Al866465, Al310575, Al580428
15 - 206	15 - 240	15 - 504	15 - 531	15 - 572	15 - 222	15 - 333	15 - 307																		•										
1 - 192	1 - 226	1 - 490	1 - 517	1 - 558	1 - 208	1 - 319	1 - 293																	-											
679414	546469	761758	421550	836390	530742	506739	967408								_																				
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HTLAC81	HTLAC87	HTLAD21	HTLAD38	HTLAF84	HTLAV67	HTLBD12	HTLBESS																												

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A1349226, AL046595, AL040694, AA493647, AI537837, AW403717, AA974049, AL036618, AL034645, AL034646, AL034646, AL03463, AL034665, AW163834, AL03464, AL034646, AL034634, AL034665, AW163834, AL03464, AL034634, AL034646, AL036073, AL034665, AW163824, AL036073, AF065135, I48978, Z72491, AF113690, AL035458, AL1313104, AF11361, AR000496, U39656, X70685, M86826, I89947, AC08913, AC08910, I26207, AL117585, I89931, AR000496, U39656, X70685, M86826, I89947, AC08913, AC08910, I26207, AL117584, I89931, AR000996, GA9996, CA113070, AL122005, AL13738, AL117457, AL113568, AF132076, AL102210, AF097996, AF118070, AL122008, U68233, I92592, AL137712, AL080137, AL117394, E01614, E13364, A07356, M9747, I48979, X53587, AL080060, AF114170, AF118064, AL133081, AL132878, AF017790, AL122098, U68233, I92592, AL137712, AL080137, AL117394, E01614, E13364, A07356, M92439, AB016525, AF113677, I42402, AL030013, AL13705, AF087790, I89934, AF087943, E02251, AB019565, A65341, X62580, AL122111, AF210052, AL137560, AL133640, X87282, AL000937, AF09506, AF118090, AF192557, AL096744, U78255, Y08769, X63574, A21103, S76508, AF113019, AL133593, AL039466, Z37987, AL137669, AL133640, X872128, AR111012, S670539, AL137639, AL137649, AL137649, AL137641, AR10221, AL13764, AF176651, AB007812, E06743, AL080158, AL137656, AL137634, AL13764, AR13764, AR13764, AR137649, AL137649, AL137640, X77287, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133094, AL133095, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137649, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654, AL133093, AL137654,	H03896, AA788921, AA985315, and AL133595.		AA132777, AA809070, and AI799864.	AI028227, AI798166, AI968058, and AI962770.	
	15-481	15 - 742	15 - 201	15 - 1162	15 - 112
	1 - 467	1 - 728	1 - 187	1 - 1148	1 - 98
	780116	1991/6	527942	559116	772644
	1395	1396	1397	1398	1399
	HTLBE82	HTLBF14	HTLBG83	HTLCA95	HTLCG77

HTLCX76	1400	767667	1 - 265	15 - 279	AL045710, and AL096749.
HTLCY27	1401	682208	1 - 288	15 - 302	W92263, AA736600, A1962876, A1539379, A1672273, AL045130, A1656897, AW001387, and A1806122.
HTLCY54	1402	908832	1 - 1050	15 - 1064	AA453366, AI188219, AI638044, AA983750, AI219830, AA453265, and AA912820.
HTLCZ48	1403	572959	1 - 399	15-413	
HTLCZ96	1404	815897	1 - 459	15 - 473	AW139921, AA725842, AI971598, AI651885, AA453466, AL110422, AI027229, AI026797, AA778573, AI279962, AI073425, AI208767, H55405, and AL118498.
HTLDA58	1405	828115	1 - 259	15 - 273	AA948538.
HTLDE53	1406	780842	1-610	15 - 624	AA400498, AA400590, AA861265, AA398875, AI149809, AI198885, AA435582, AA460749, AA460151, AA889548, AI015434, and AA815269.
HTLDE64	1407	908613	1 - 838	15 - 852	
HTLDE95	1408	616724	1 - 285	15 - 299	AA566051, AA5522211, AA393552, AA418209, H05646, H06920, R34733, AA293017, ZA2496, AI743990, and AA280537.
нтсрезз	1409	909254	1 - 616	15 - 630	AI376558, AI208582, AI149687, AI028197, AA629337, AI027966, AI202003, AA694500, AI701718, AW207552, AI336775, AI560530, AI215526, AW207059, and AI015601.
HTLDG55	1410	911645	1 - 196	15-210	
HTLDH65	1411	839795	1 - 901	15 - 915	N47989, AI675771, AI024189, AI651589, AI621081, AW003588, AW293606, AI026721,
					AA954294, N51195, and AA983886.
HTLD190	1412	835850	1 - 458	15 - 472	AB020719.
HTLD094	1413	915223	1 - 542	15 - 556	AA860341, AA889689, AA730148, AA478113, AI024743, AA730132, AA082366, and AA758028.
HTLDP77	1414	920246	1 - 638	15 - 652	AC002128.
HTLDQ25	1415	870057	1 - 1220	15 - 1234	AA399278, AA889597, AA758803, AW117336, AA398195, AA729781, AA889586, and AA922590.
HTLDS55	1416	891322	1 - 1302	15 - 1316	AI890919, AI018797, AA913452, AI797580, AI809012, AI187382, AA448485, AI554914, AW137847, AI393577, AA382830, AA432050, AA609003, and AC020663.
HTLDT05	1417	909752	1 - 473	15 - 487	R59447, R17647, T62170, and AI439348.
HTLDT81	1418	952265	1 - 480	15 - 494	AA398001, AA399683, AW177623, AA809773, and AL137531.
HTLDU05	1419	911649	1 - 589	15 - 603	AA437044, AF113527, AB023062, and AF113520.
HTLDV31	1420	867748	1 - 297	15-311	
HTLDX88	1421	791684	1 - 686	15 - 700	
HTLDY85	1422	573746	1 - 481	15 - 495	
HTLDZ14	1423		1 - 334	15 - 348	
HTLEB14	1424		1 - 402	15-416	
HTLED72	1425	686906	1 - 273	15-287	

		294160.			M62294	A1044506	AA442457 AA601101 ACONS615 224 ACONSE188	AC003976 AC005702 AC005662 228 AT 112264	AF042793. AB011130. AF042702. AE040700. 0-4.284.02.	2011 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0	AA250913. W56681 R24100 H01201 A 4 161224 A 111 C0800	AI760165, AI341569, AW241888, AW135684, AI624778, AA883817, AI494564, AA772107	AA521079, and AA405142.	Z68869.	AA305510, AA099550, AI917501, AI631488, AI142135, AW391262, AA305581, N39659,	A1525/21, and AF151810.	AL1330/1.		AI207997, and AW172597	A1968198. A1655275. AA397907. AT 044110. AWADASC2. AT 044115	AL041695, AA454137, T19069, D31407, and AT 122562	1000 1000 1000 1000 1000 1000 1000 100	AI808336, AW013835, AI674717 and AI650A08	AA776758, AI808140, AA884694, AA909615, AA904970, AA909196, AW294544, AA723919, and AI525608	D02014	A1.122017.		AC005343	AC000097 AC006547 AP000344 2-4 AC00542	DS1002 A1541205 A1541321 A1557082 A1525660 A155568	AI525500, Z33559, T18597, AI557533, AI557731, AI555666, AI55753, T16697, AI557602,	AI525757, C14322, D50992, AI525856, AI557241, AI541027, AI525857 AI535630 A A A A A A A A A A A A A A A A A A A	AI540903, AI541365, AI557084, AI541048, N71206, AI557312, AI526728, AI55731,
15-323	15-1181	15-113	15 - 556	15 - 477	15 - 970	15 - 308	15 - 332	15 - 529	15 - 107	15 - 595	15 - 145	15 - 457		15 - 349	15 - 581	16 606	000 - 61	15 - 217	15 - 326	15 - 1110	15 - 826	15-113	15 - 275	15 - 588	15 - 348	15 - 325	15 - 350	15 - 226	15 - 336	15 - 382		-	
1 - 309	1 - 1167	1 - 99	1 - 542	1 - 463	1-956	1 - 294	1-318	1-515	1 - 93	1 - 581	1 - 131	1 - 443		1 - 335	1 - 567	1 - 502	720-1	1 - 203	1-312	1 - 1096	1 - 812	1 - 99	1 - 261	1 - 574	1 - 334	1-311	1 - 336	1-212	1 - 322	1 - 368		-	
870258	870154	870257	934287	573460	973302	960314	506747	917022	575080	953712	056699	719160		506649	574942	9633706	00/00/	573403	574884	911654	836820	573454	527956	883332	870255	573458	967309	775310	791662	934288	_		1
1426	1427	1428	1429	1430	1431	1432	1433	1434	1435	1436	1437	1438		1439	1440	1441		1442	1443	1444	1445	1446	1447	1448	1449	1450	1451	1452	Н	1454			
HTLEF94	HTLEG65	HTLEG91	HTLEH30	HTLE147	HTLEIII	HTLEJ93	HTLEK64	HTLEL01	HTLEL03	HTLEL07	HTLEL31	HTLEM46	0 % O % O	HILEOSO	HTLEP16	· HTLEO07	1177 770.43	HILES43	HTLES54	HTLET56	HTLET78	HTLET93	HTLEV33	HTLEV95	HTLEW12	HTLEW21	HTLEY11	HTLEY91	HTLEZ14	HTLEZ15			

AI525302, Z33585, AI541075, AI541034, AI541346, AI541353, AI541154, AI557039, AI557041, AI557222, AI557317, AI525656, AI546829, AI536070, AI535813, AI525666, AI541056, AI535994, AF025310, Z30183, U45328, AR050070, U94592, A82593, A63903, A62298, and A62300.	1-512 15-526 AC005899.	1-695 15-709 AA398001, AA399683, AW177623, AA809773, and AL137531.	1-1029   15-1043   AA356490, R05624, AA262044, and AL138430.	1 - 591 15 - 605	1 - 1305 15 - 1319 AW275845, AI830267, AI572906, AI439086, AA766499, AA723111, AA836614, AA453028, AA747738, AA483838, AA077798, AA077483, AW302599, AA215573, AA077013, AA009576, AA077510, A107751	1-463 15-477 AC006237.	1-423 15-437 AC003963.	1-616 15-630 AF053356, and AF174604.	1-501 15-515 AL117491, AB007913, AL137693, and AL110281.	1 - 329   15 - 343   AI001797, and AI910520.	1 - 1477   15 - 1491   AA608970, and AA758832.	1 - 1010 15 - 1024 AA403179, AA398239, AW339857, and AA952990.	1 - 561   15 - 575   AW269804, AA781852, AW104592, AI239999, AI698249, and AC005821.	1-470 15-484 AW393087, R16949, R75708, H44330, AA186786, AA259086, R55419, AA329264, AA335735.	AA329538, AA39356, AA354448, W93021, AA136776, T35806, T10451, R46300, R54656,		1 - 752 15 - 766 C02944, C03248, AI807681, AA095819, AI797565, AI333238, AI863457, H53759, AW138808, AW451889, AW138004, AW207397, AW184023, and AC005216.	1-1194   15-1208   AI693474, AL042395, AL041671, AW168041, AI738586, AA504349, AI125391, AI990015.	AA838043, AI149664, AL041569, AI864457, AA579771, AW273185, AW294188, AW197733.	AI805280, AA383594, AI699335, AI138789, AI653680, AI738485, AA383400, AI475427,	AA976749, AI203057, AA883961, AI968077, AF096834, AF073954, AF073955, AC003688,		1-533 15-547 AL040693.	1 - 794 15 - 808	1 - 1358 15 - 1372 AA399144, AI982647, AA394141, AA234366, AA405404, AA034080, AA644012, AA234434,	1-752 15-766 A173R485 A173R586 AF006R34 AF003688 AF073055 2nd AF073054	20.
	870261	934172	917128	917033	954984	934278	775392	953730	781303	573462	870136	835493	789656	868309		-+		952254					918606	958208	870528	908428	
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	HTLEZ32	HTLFA74	HTLFC20	HTLFE01	HTLFE05	HTLFE20	HTLF128	HTLF139	HTLF183	HTLFJ39	HTLGD25	HTLGD69	HTLGG36	HTLGK55			HTLGM02	HTLGM07					HTLGT62	HTLGW17	HTLGX90	HTLHC14	

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15-957	15 - 574	15 - 1752		15 - 532	15 - 879	1511-51	15 - 1801		15 - 260	15 - 283																_				
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953729	934279	922923		967336	953714	924755	922994		835652	723331			_																	
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	15 - 318	15 - 574	15 - 263	15 - 306	15 - 261	15 - 310	15 - 270	15 - 327	15 - 266	15-316	15 - 325	15 - 177	15 - 427	15 - 392	15 - 126	15 - 253	15 - 1309	15 - 307
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HTTDF90	1523	917155	1 - 427	15 - 441	AW052029.
HTTDG36	1524	968131	1 - 347	15 - 361	
HTTDI21	1525	869686	1 - 341	15 - 355	
HTTDJ65	1526	973307	1 - 406	15 - 420	AC006030, AP000513, AB023052, and AC006140.
HTTDL38	1527	573641	1 - 289	15 - 303	
HTTDL45	1528	523452	1 - 291	15 - 305	AW292800, and AC007390.
HTTDL89	1529	959837	1 - 328	15 - 342	W22023, AC004765, and AB002342.
HTTDN40	1530	734318	1 - 373	15 - 387	AA182963, W39759, AA132990, H69405, R94355, T66121, H68623, H68650, N36314, R14727
					AA166770, R70624, AA923755, AW385783, R69735, AA190899, R19750, T10743, H07954, H93885, AA164319, and AC005876.
HTTDN85	1531	783444	1 - 435	15 - 449	AL137653.
HTTD019	1532	908937	1 - 320	15 - 334	
HTTD037	1533	573685	1 - 431	15 - 445	
HTTDR91	1534	790336	1 - 549	15 - 563	AA252780, T84947, and AC005740.
HTTDR92	1535	273666	1 - 326	15 - 340	AC003046, AC002366, and AC003685.
HTTDS02	1536	920589	1 - 418	15 - 432	
HTTDX84	1537	921100	1 - 668	15 - 682	AA432195, AA435548, and AA431175.
HTTDZ54	1538	692608	1 - 286	15 - 300	AW163244, H89834, W06845, N42782, N42829, N31946, and A1190785
HTTDZ91	1539	523206	1 - 300	15-314	AI762137, AW242639, AA044752, AA884207, AA235512, AI870472, DR0100, D59403
					W88874, AA481286, N92013, D31111, D31113, A1167596, R10048. AA906542, AW087683
					R49500, AI361492, AF155112, and AL137478.
HTTEB33	1540	573719	1 - 336	15 - 350	
HTTEH58	1541	747943	1 - 307	15 - 321	
HTTEL50	1542	745985	1 - 196	15-210	
HTTEU68	1543	967819	1 - 1207	15 - 1221	AA134604, AA187575, T75572, AA083163, W42892, A1092672, T97891, 244468 R34642
					R14267, AI078644, AA354837, R48102, AA362636, R55924, AA497072, AW044159,
					AW377397, R17450, T78498, AA625142, R56338, AA258076, and R99732.
HTTEV62	1544	573614	1 - 272	15 - 286	AI828837, AI015418, and AA953392.
HTTEY64	1545	974107	1 - 450	15 - 464	
HTTEY67	1546	917903	1 - 1523	15 - 1537	AI869330, AW295435, AI208233, AA447451, AA844516, AA664002, N40294, W04890, AI925298, AA903925, AA447450, AW243078, H14692, H14687, AA36630
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HTTFA16	1548	870198	1 - 394	15 - 408	AA160412, and D78751.
HTTFB60	1549	999698	1 - 208	15 - 222	AW298813.
HTTFG35	1550	778426	1 - 254	15 - 268	AA581033.

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HTTFM66	1556	950051	1 - 1145	15 - 1159	AA085574, AA490803, AA147472, AI239866, and AL049745.
HTTFS59	1557	825922	1 - 842	15 - 856	AA228367, AA176965, AA228376, AA004521, AA251249, R00504, AA303183, AW136898
					AA448887, R00605, AA229970, H50956, AA345572, AA040486, AA004604, AA177117,
					AW247896, 174926, AA566080, and AF045584.
HTTFT08	1558	934460	1 - 441	15 - 455	
HTTFV93	1559	925544	1 - 393	15 - 407	AA301328, and H78684.
HTTFW03	1560	923105	1 - 459	15 - 473	AC006566.
HTTFX21	1561	924775	1 - 580	15 - 594	AI632236, AI279533, AI339379, AI806232, AA401419, AI356680, AW051296, AI096764
					AA401395, AW008336, AI419077, AI423753, AI276550, AI435531, AW205745, AW104726.
					R60187, AI081767, AA830892, AI917002, AI806411, W03327, AW134602, H72137, H71911.
					H66942, H79399, AA507360, H66943, H81492, AA847135, H71435, H71434, A1824610,
					A1652697, AA829202, H72050, N32176, H71912, AA507323, H79288, R83711, AA886536,
	]				and A1022603.

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1-357	1 - 592	1 - 1053	1 - 390	1 - 472	1 - 328	1 - 765		_				•									1 - 539	1 - 573	1 - 434	1 - 418	1 - 406	1-417	1 - 297	1 - 271	1 - 397		1 - 375	1 - 430	1 - 434
974066	931004	953479	926752	869636	869635	934089		_									•				869634	931015	922817	930994	839725	869618	869615	913799	934130		974063	958170	948750
1562	1563	1564	1565	1566	1567	1568															1569		╗	$\neg$	1573	1574	1575	1576	1577		$\dashv$	1579	1580
HTTFZ70	нттнноѕ	HTTHU43	HTTIG04	HTTTH23	HTTIH80	HTTIL06	<del></del>	_							<del></del>						HTTIN23	HTTTU05	HITIW81	HTTIZ05	HTTJA11	HIIJA4/	HITIHI3	HTTIM01	HTTJQ06	O / A PARTICIPATION A	H1117X68	HIIIJY08	H11KD44

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1-411	1 - 378	1 - 584	1 - 464	1 - 504	1 - 487					1 - 562	1 - 470	1-416	1 - 214	1 - 366		1 - 294	1 - 335	1 - 296		1 - 309	1 - 258	1 - 212	1 - 371	1-315		1 - 334	1 - 240		1 - 546	-	
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	1 - 340	1 - 168	1 - 352	1 - 289	1 - 98									1-330		1 - 266	1 - 353	1 - 358	
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	HUVFC07	HUVFH03	HUVFH32	HUVF103	HUVFK11

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	933167	Н	913996	<del>  </del>	925793	957658
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1693 1694 1695	-	15 - 436	AA298987, and AC006222.
1694	1 - 467	15 - 481	AA528216, AI347038, AI308941, AA583432, AA412292, AI147693, AA632915, AA836857,
1694			R42401, H17978, AA299011, AI207239, AA349833, AA494556, F12523, AA290708, and AF184971.
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			AASS9241, AL908575, AL119724, K43288, AA833896, AA833875, H12383, AA402129,
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		HUNAB76	HUNAB42	HUKFS69	HUKFL89	nort/1				

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	1 - 480	1 - 367	1 - 393	1 - 296	1 - 436	1 - 336	1 - 246	1 - 112	1 - 385										1 - 337	1 - 367	1 - 315	1 - 636	1 - 390	1 - 146		7:5	1 - 310						
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HUKAB63	1728	625273	1 - 195	15 - 209	AI079608, AI807065, AI952291, AI590123, AI090727, AI016788, AA456134, N20016,
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HTTEX05	1746	931024	1 - 520	15 - 534	AI493098, AW024745, AA921917, W90789, and AI915946.

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15 - 355	15 - 571	15-815	15 - 441	15 - 350	15 - 272	15 - 373	15 - 553	15 - 564	15 - 472	- 1	15 - 162	15 - 777	15 - 506	15 - 387	15 - 748	'	15 - 403	15 - 406	15 - 370	15 - 422	15 - 324	15 - 483	15-497		15 - 238 I	15 - 343	15-615	15-436	15 - 207 I		15 - 258	15 - 436 F	15 - 313
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974323	926772	965920	958169	895696	944914	751809	742004	739445	917156		900662	728344	273669	932294	744438		460948	694222	_	784537	796674		960599		524841	714220	932997	780164	925409	781590	530559	767520	530567
1747	1748	1749	1750	$\overline{}$	_	1753	1754	1755	1756		1757	1758	1759	1760	1761		1762		-	1765	1766	1767	1768	+	$\dashv$	1770	1771	1772		$\dashv$	$\dashv$	┪	1777
HTTIR33	HTTIR04	HTTINIII	HTTIE08	HTTIB12	HTTHJS6	HTTFG12	HTTEZ61	HTTEQ59	нттео01		HTTEO59	HTTE053	HTTEJ56	HTTEB05	HTTD059		HTTDM42	HTTDL81	HTTDL75	HTTDA85	HTTCQ95	HTTCJ39	HTTCD06		HTTCB87	HTTBR42	HTTBP62	HTTBO82	HTTBM03	HTTB180	HTTBH95	HTTBH75	HTTBH36

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HTTAN34	1782	509454	1 - 455	15 - 469	AA252276, AA227154, AI656990, AA301077, AA301076, AL042627, AC004593, AL023574, and AC007536.
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HTTAH03	1784	965134	1 - 282	15 - 296	AI198425, AI480040, AW054766, AI564875, AI359129, AI359233, AI422375, AI651642
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HITAC//	58/1	772735	1 - 764	15 - 778	AI694695, AA913353, AW236100, AA846529, AW301152, N62629, AI366198, AA449338,
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HTTAA94	1786	793001	1 - 555	15 - 569	AA191546, W91892, AA486427, AA694339, AA416561, AI140707, AA417297, H77647.
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HTTAA39	1787	710355	1 - 284	15 - 298	AI800489, AW105035, AI480088, AW299975, AA303221, AI670831. and AA135748.
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HTT HS05	1704	033770	1 712	15 775	7410006, 4100116, 4100106, 4100109, AR/81021, and W04559.
COCHITILI	1/2	733120	1 - / 12	07/ - C1	A1348086, A1928136, A10/4838, AW 136076, AW 243178, A1262696, AA627913, A1810972,

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		AL036150, D81111, Al910186, D80164, D59627, C14389, H00072, C15076, D59467, D51060.
		AA305409, AL036268, AW178893, D51213, D51079, C14298, AL038043, N47620, D80251,
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		A38214, A98767, AR031374, 156772, 195540, AR018924, A49700, A63067, A51047, A63064,
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		E01718, E02003, E02102, E03550, A28163, E02100, E01997, A58998, E02291, E02292
		E02293, E01999, E02396, E02327, E01563, E02431, E01693, E01696, A92668, AR005163,
		AR005154, AR005157, AR005160, 109250, AR005153, A92667, E01024, AR050583,
		AR050584, E02430, E01148, E12527, E01503, AR005165, E12523, E02432, A49701, A62009,
		E01216, 177211, A95096, 170974, 131847, 131848, AR060673, AR060676, A95106, A95105,
		A80476, A91965, E01324, 108638, A80474, A94048, A94061, A80477, AR035224, A80475,
		A34040, A34034, 103500, AR031529, A49428, 163561, 163563, and E16036.

HTEMS01	1854	915308	1 - 576	15.500	AW187180 ATTEST ATTEST ATTEST ATTEST ATTEST ATTESTS ATTEST ATTESTS ATT
				2	and AL049761.
HTEMO58	1855	964769	1 - 475	15 - 489	AI026760, H54090, W90174, AI016127, and U22296.
HTEMN80	1856	775543	1 - 301	15-315	T80539, and AI719083.
HTEMM91	1857	938396	1 - 378	15 - 392	AI655972, AI809237, AI872211, AI377032, AI381901, AA523409, AI150552, AI248517,
	_	•			AW328508, AA523391, AI241274, AA609120, W92335, AW194863, AA580479, AI912966,
					AW243314, Z25384, AI217725, AA531424, AI142666, AW137703, W56565, W56787,
HTEMISI	1858	870613	1 - 592	15 507	A11/0/91, F1/360, K93131, AW03/331, and A1823/87.
TO THE PARTY.	201	010010	1 - 200	160 - 61	A1149800, and AA918102.
HIEMBS/	1859	849214	1 - 456	15 - 470	AA398093.
HTELY90	1860	787549	1 - 356	15 - 370	AI022425, and T86122.
HTELV29	1861	806421	1 - 627	15 - 641	AA083981, AL043302, AL050276, AF194030, and AF185576.
HTELP07	1862	952274	1 - 550	15 - 564	AI005651, AA502325, and AI005304.
HTELM71	1863	954982	1 - 509	15 - 523	AA843728, AW303661, and AA813137.
HTELA02	1864	618699	1 - 602	15-616	AI651239, AW268856, AI024356, AI016924, AI016923, AI698585, AA609414, AA620051
					AW072208, AI696034, and AI340253.
HTEKU62	1865	754010	1 - 713	15 - 727	R13043, AA402245, W03238, and AA293855.
HTEK162	1866	812862	1 - 472	15 - 486	AA741257, W23913, AA769417, AI923864, AA099994, AA113016, AI633572, AI129921.
					AI740509, AI087861, AI198728, AA451698, AA811514, AW328432, AI345992, AW135872.
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					AI864067, AI992065, AW027054, AI129952, AW105702, AA527064, AW166911, AI969997
					AW263370, T12481, AI571406, AW243885, AA192190, AW134596, A1143876, A1143870
			-		AW136628, AW009874, AI475650, AA063520, F21628, AA781441, F37014, AW074003
					A1928446, AA736768, N91862, AA774271, A1611242, AW363815, F33207, AW328431
					AI470616, H39778, W76151, W72588, AW44846, AW368798, AI479056, AI861919.
					AI223368, AI760686, AA973718, AA991724, AA804626, AW449436, AI217528, AI246328.
					AI391628, AA977169, AI222649, AI453599, AI825699, AI968087, AA910938, AW294100,
11777777	2,01	70,000		,	N74597, AI587076, AI738417, AI818572, AI347378, and C00207.
nienni)	190/	947270	1 - 043	15 - 657	
HTEKD77	1868	772397	1 - 414	15 - 428	N47372, AA029276, AW173125, T51928, AW197647, AA436376, N56847, A1142573,
					AA885319, W26719, AI961121, R52187, AI032543, AW009278, T51718, AA992217, W37315,
					AI370687, AA495856, AI073556, AL041264, AF147339, and AP000533.
HTEJV94	1869	793039	1 - 381	15 - 395	AI628611, AA416585, AA420969, AW271467, AI831883, AI928360, AA421125, AW001638.
					AA397955, AI656005, AW016672, AW003460, AL110224, and AC003669.
HTEJ046	1870	717850	1 - 388	15 - 402	R72953.
HTEJN12	1871	653252	1 - 443	15-457	AA223373, AL096763, and Y18004.

R92318, R97141, D61526, W58524, R13204, AA333107, AW163212, R55599, H23092, D52777, A1929587, C05240, R19781, D61319, AA150352, Z46053, AA355121, AA296708, AA323111, D53669, R26633, H08329, AA317832, AA322876, W01316, AA973604, AA374431, R49663, AA296782, H253781, AA149563, AA318184, A1368381, AW088920, A1253781, R40292, A1928933, A1857794, A1452755, A1160425, AA975568, AA961868, A1718865, AA776210, AA025635, AA337795, A1191849, W73632, N79435, AA679726, AA865487, W78161, AW339133, A1582690, W58412, A1744177, AA902205, H97698, A1338657, A1338667, AW452422, A1187166, AA330474, AA333363, AA976009, AA126618, AJ239435, A1572582, AA085720, R55362, AA360533, AW166355, A1879369, AW16076, AW403792, AA111927, D61306, N31004, AA064830, W79204, D53612, AA961222, AA845309, AA186387, W07796, W73680, N58648, AA642523, AA151815, A1805801, T30103, D54012, T36033, AA393418, AF092135, and AL,109701.	R94482, and A1004651.	AA993947, AW134645, AA884829, AI004532, AI150514, and AI239661.	AI002739.	AI208897, AI187424, AA682756, and AI187850.	R72964, W76526, R64535, and U82396.	AA417003, AA835058, AI424995, AI220270, AA694436, AW182313, R20520, AI382131, A1004786, AA418740, AA418795, A1190974, 738070, AA74555, and A 100074	N71729, N71226, AP000041, AP000109, and AP000085		AA724539, and AA960890.			N38963, and R92356.	AW451115, AI863336, AW104507, AI692981, AI652017, AI827145, AI017283, AI955549, N33485, R76560, AW409808, AI207003, AI202422, and AI977781	AA916546, AI204535, and AL021331.	AA424196, AA846387, AI797455, AA778547, AW340809, AI217364, AI188208, AI150580, AI123441, AI027637, AA770175, AI150190, AF012356, AA909271, AF012355, and AA442327.	C04728, AA381098, N45678, AA480568, W69682, AA397755, AA476511, AA476550, AI860245, AW024421, AW382036, AW382039, AA838817, AW382042, AW382041, AW381999, AW382041, AW381961, AW382000, AW381997, AA934010, AI363359, W69923, AW190584, N36268, W44317, AA181315, AI864889, AA130883, AI745226, AI934734
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1 - 386	1 - 587	1 - 451	1 - 371	1 - 390	1 - 403	1 - 425	1 - 528	1 - 247	1 - 318	1 - 336	1 - 223	1 - 489	1 - 442	1 - 561	1 - 391	1 - 242
696784	490772	953801	887112	870660	684711	708304	491030	395868		-		734983	734976	967439	664436	964956
1872	1873	1874	1875	1876	1877	1878	1879	1880	1881	1882	1883	1884	1885	1886	1887	1888
HTEJL30	HTEJC70	HTEJB07	HTEIS34	HTEIS25	HTEIN26	HTEIL36	HTEIJ58	HTEID15	HTEIB38	HTEIB37	HTEIB03	HTEIA57	HTEHX57	HTEHV11	HTEHS17	нтвнии

AA187057, W38774, AW382054, N26942, A1469219, A1380284, A1380273, W45689, A1057575, AA725447, A1360479, N48961, and A1057565	15 - 1020 AI288698, AI914273, AI203577, AI696478, AA913934, AA812691, AI573252, AI936975, AI015501, AI280024, AW054753, AA975903, AI371833, AI160502, AA844728, AA687959, AA393300, F34643, AA813782, T53463, AI091343, AA435624, AA595143, T53462, AI364294, and AI217827.	15 - 390 R61288. R05576. AA778664. AA280073. AB014581. and 708752	15 - 612 AA256743, AI374955, AI123527, AA251700, AA455406, AA429834. AA618437 728611	AI433315, AA331686, AI498096, AW203957, AI377211, AA770064, AA808245, AA828466,	AA098810, AA331825, AA814045, AA101241, AI078061, AA625885, H53435, AA357747,	15 - 488 R13795, and R14717.	15 - 621 N32789, AA992305, AI829630, AI453589, AI037906, AA490671, N47354, AF106857 and	AF026169.	15 - 370 W87922, and AA694342.	15 - 221 A1125270, A1025275, A1017509, AA724721, AA970833, AA904629, and AC002128	15 - 477 N51343, AI341075, AI967945, AL035252, Z79996, AL031775, AL021978, AC002384 and	AC002455.	15 - 582 N41791, AI734225, W21309, AF026169, and AF106857.	15 - 637 AA011636, AW136535, AA641738, AI242200, AA972854, AI357112, AI252660. AI919234.	AI732405, and AW379801.	15 - 551 AA188885, AA189066, AA834951, AA971947, AW389450, AA856992, and AA189065	15 - 484 N78395, and H45135.	15 - 341 AL044999.	15 - 116 AC004259, and AC004600.	15 - 289	15 - 362   AA442512, AA002017, N68854, AF122013, AF064102, AF000367, and AF064103	15 - 385	15 - 409 N55308, AI201311, and AA709195.	15 - 343 AA461517, AL040379, AI825108, AL040378, AC007981, AC011718, AC008103, AC012330,	AC007708, AC007324, AC009288, AC008079, AP000550, AC007325, AP000552, AC008018,	15-340 H53320 R97852 A1032585 H53321 R07802 A1033531 CLA A103434	15 - 260 AC005726.	1
	1 - 1006	1-376	1 - 598			1-474	1 - 607		1 - 356	1 - 207	1 - 463		1 - 568	1 - 623		1 - 537	1 - 470	1 - 327	1 - 102	1 - 275	1 - 348	1 - 371	1 - 395	1 - 329		1-326	1 - 246	
	920628	931017	932987			765901	732630		709420	545137	866069		887616	666920		719280	685383	530196	707717	575476	530203	530200	675071	677513		780161	530201	
	1889	1890	1891			1892	1893		1894	1895	1896		1897	1898		1899	1900	1901	1902	1903	1904		1906	1907		1908	1909	
	HTEGW02	HTEGUSS	HTEGS24			HTEGJ74	HTEGJS6		HTEGI38	HTEGH60	HTEGC30		HTEFX90	HTEFU18		HTEF046	HTEF028	HTEEU78	HTEEU35	HTEEU27	HTEEU18	HTEEU17	HTEET22	HTEEF25		HTEEB82	HTEDX39	

HTFDX03	1011	1975767	1 100	15 204	AWOODS A ACOUSTON AND A CONSOLAR
HTEDW96	1912	881958	1 - 190	15 - 553	AW002641, AC005500, and AC006946.  AA101046 AA860334 A1240068 A1381744 AA064650 M70134 AD006636 AE133603
					A86973.
HTEDW59	1913	530448	1 - 201	15-215	AI139615, and AL117627.
HTEDV86	1914	785818	1 - 497	15 - 511	W87362.
HTEDUS3	1915	727362	1 - 443	15 - 457	N75217, A1827641, and AI313263.
HTEDS40	1916	934047	1 - 496	15 - 510	N64316, and AA418089.
HTEDS06	1917	960645	1 - 839	15 - 853	AA557354, AA004230, AA702179, AI671185, AI924143, AI609113, AI056239, AI638795.
					AI337375, AA634413, AW250803, AA417152, AL135398, AA478510, AA195614, AA190630
_					AI814763, AA827285, AI091408, AI638180, AI080126, AA632206, AI379107, AI288872,
					AI263619, AA626405, AI679151, AI754325, AI769841, AI559213, AI679722, AA417030,
			*****		AA552345, W93249, AA007263, AI969543, AA766364, AA534494, AI038181, AA960978,
					AA449336, AA573241, AW043937, AA725439, AI291838, N73539, AA189108, AI699813,
					N73585, AW104716, AW166044, D19671, AW192890, AA454518, AA621586, H73339,
					N54283, AA910989, H14801, H05808, N56013, H75580, AI038699, AA248270, AA149737,
					H70079, AA808510, AI806228, AI806407, AI628327, AL079833, W93248, AA478509, and
UTEDO75	1010	160626	107	16 100	AF044588.
11120013	1210	10/024	1 - 104	13 - 198	
HTEDK72	1919	766343	1 - 339	15 - 353	AI693509, and H95965.
HTEDJ92	1920	522827	1 - 294	15 - 308	
HTEDJ63	1921	980805	1-310	15 - 324	Z98257.
HTEDI09	1922	522969	1 - 397	15 - 411	AI797509.
HTEDI01	1923	_	1 - 230	15 - 244	AC006960, AC005015, AL035249, and AL049569
HTEDH90	1924	909165	1 - 403	15-417	R79137, AA314329, AA323430, U69560, AC007731, and AC005500
HTEDH76	1925	522940	1 - 208	15 - 222	AC004945.
HTEDH42	1926	615250	1 - 459	15 - 473	C03196, C03292, F00515, AA361228, AW003009, AA626353, AW403239, W67213.
					AA314421, W05346, W63719, AI346486, W24987, D12319, D11537, AA423922, N45183.
					AR053393, and AF092130.
HTEDH30	1927	522936	1 - 237	15 - 251	AL049697.
HTEDH17	1928	522938	1-371	15 - 385	
нтерн06	1929	869427	1 - 392	15 - 406	AC006251.
HTEDG75	1930	890715	1 - 358	15 - 372	
HTEDG26	1931	519947	1 - 384	15 - 398	AW246994, AA421090, AA421091, AA397662, AA375279, R83399, AI638717, AA306667, AA747622, and AC000378
HTEDF96	1932	614726	1 - 323	15 - 337	AA242852, AA252186, AI129391, AA743400, AI934605, AA531278. AA705950, AA418351
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AA834128, and AC006942.	AI656191 221249 and 221248	8, Z83843.		AW241925, and AC005232.	N80927, AA400153, AI027600, W58447, AA813400, AA746206, AI139801, AA828177, AW175643, AI279610, AI350755, AA444123, AA443044, AA56017, AA451605, AI050230	AI632987, AI338403, AI262825, AA767495, AI005034, AA453635, AA454013, AI560993.	AW250814, T30813, AW149100, AW327945, AW207031, AA629893, AI342923, AA922333.	F37015, AI745194, AA676942, AI086189, AI276499, AW058509, AI682025, AW004973,	AW009042, AI367703, AI445623, AI241535, AA441932, N73089, AW295548, AI188497,	F04870, F10561, W58482, Z41848, T35208, AA548624, AI094343, AA923598, AW440500,	W76342, AW080667, AI720047, T17396, R37034, F22096, R39180, AA833987, AA197182,	AA426126, AW363378, AI797280, AA196359, T19458, AI743371, AA090309, R34367,	AA446271, T61317, AW407104, N71508, AA075086, AA383602, C21530, AI371957,	AA192312, N22129, N91820, AA374751, AA213591, AA813578, H43284, H97310, C00318	T10425, T98391, AA832076, AI049609, AA740854, AA349688, AA369853, and AL035405					AI025190, AL137266, AC005071, AC005488, AC004878, and AC006014.	AA804334, and AW007980.						AA406427, H66890, H64867, H66639, H69191, AA693972, AA410436, AA931060, N38830,	H48140, AI247909, AA251684, N23377, N76083, AA887276, T61107, AW328038, AI681235,	AW328039, AA608986, H72100, N71448, AA188574, C02442, H70867, R94076, AA394213,	AA487534, T68446, AC005185, AL121877, AC006039, AL121578, AC006458, AC005544,	AC005014, Z84481, AP000261, AP000100, AP000035, AC004696, AC002094, AC008040,	AC003774, AC000137, AC003284, AL049834, AL080250, AC006150, AF048727, AL022393,   AC004448, AC007001, AF129077, AF165147, AC008009, AC004202. AP000518. AC002383.
15 - 308	15 - 370	15 - 305	15-417	15 - 421	15 - 557											15-315	15 - 403	15 - 298	15 - 435	15 - 332	15 - 356	15 - 338	15 - 342	15 - 192	15 - 416	15 - 384	15 - 331					
1 - 294	1-356	1 - 291	1 - 403	1 - 407	1 - 543											1 - 301	1 - 389	1 - 284	1 - 421	1-318	1 - 342	1 - 324	1 - 328	1 - 178	1 - 402	1 - 370	1 - 317			-		
779775	742368	908406	522997	523002	789732											870723	650885	508104	960428	527210	527214	527203	533795	527209	523029	508142	508124					
1933	1934	1935	_		1938											1939	1940	1941	1942	1943	1944	1945	1946	1947	1948	1949	1950					
HTEDF70	HTEDF60	HTEDF22	HTECE66	HTECE62	HTECE61											HTECE51	HTECE39	HTECE31	HTECE08	HTECD94	HTECD88	HTECD70	HTECD65	HTECD56	HTECD15	HTECC71	HTECC45					

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15.417	15 - 367	15 - 355	15 - 441	15 - 422	15 - 750	15 - 318	15 - 292	15 - 369	15 - 422	15 - 574
1 - 403	1 - 353	1 - 341	1 - 427	1 - 408	1 - 736	1 - 304	1 - 278	1 - 355	1 - 408	1 - 560
508144	678659	960439	508135	508132	728811	715704	503275	578544	921321	870732
1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961
HTECC26	HTECC09	HTECC08	HTECA44	HTECA39	HTEBP54	HTEBO43	HTEBM87	HTEBL53	HTEBJ02	нтевно9

					AA781035 AA735508 AA758847 AI671537 and AI135354
HTEAX06	1962	960792	1-413	15 - 427	AW300891, AW182267, AI002121, AI393590, AW268430, AA812869, AI363725, AI937132, AI370331, AA431750, AA383228, C20655, and AI537879.
HTEAV22	1963	679394	1 - 449	15 - 463	H16258, AI362696, AA159083, AI337351, AI049674, H05276, AI963664, AA612853, AA421018, R50945, AA398617, AI276451, AA868365, and AA383003.
HTEAU39	1964	503295	1 - 428	15 - 442	R45446, AA994896, AI285099, AI419926, AI219508, AI650680, R41613, AA383142, AI264406, AI942371, and AC005752.
HTEAT17	1965	667184	1 - 298	15 - 312	AA416657, AA394107, AA629341, AA382909, AI075928, AI150321, AI204602, AW022487, AA397912, AA862555, AI066604, and AA442269.
HTEAS02	1966	921323	1 - 527	15 - 541	AI203924, AA383061, AI215017, and AA861908.
HTEAR93	1961	503298	1 - 361	15 - 375	AA383056, and AA383057.
HTEAQ55	1968	732562	1 - 1106	15 - 1120	A1979276, AW117497, AW269774, AA701653, W46209, AA778787, AW269767, AI218590,
					N20493, W28100, AA039403, AA781351, AI025502, AI696076, W26315, AI281715, A A 088506 N25535 A 1220500 A W136055 A A 758081 A 406660 A 4 673182 A 153110
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1175 4 106	996	503533	100	207 21	C20812, and AC004805.
HIEAJYO	1909	203233	1-471	15-435	AA382/36, and AA382/55.
HTEAH75	1970	503546	1 - 324	15 - 338	AA382618, and AA382617.
HTEAG47	1971	503623	1 - 411	15 - 425	AA707221, H91075, AA677780, H90565, AA382495, AA382494, and AI825267.
HTEAG08	1972	960469	1 - 322	15 - 336	AW298466, AA382538, AA504454, and AA382537.
HTEAB50	1973	724751	1 - 310	15 - 324	AA459803, AA382330, AW084476, AW118229, AA770485, AI393130, and AA894604.
HTEAA04	1974	925522	1 - 533	15 - 547	AA431127, AA432144, and AA382138.
HSWBY36	1975	708291	1-413	15 - 427	AA993042, and N22565.
HSWBT69	1976	867537	1 - 366	15 - 380	W25339, AA046193, AA449279, and U36384.
HSWBE29	1977	412991	1 - 394	15 - 408	A1034154, A1075224, A1273184, AA912285, A1950513, A1885608, A1335673, A1887898, A1080389, AW243126, AA912258, A1656815, A1860003, AA743734, and M57280
HSWAS65	1978	953051	1 - 391	15 - 405	AI149166, AW134820, W74519, AI126334, AI458127, AI702779, AW241716, W74520
					AI313414, AA325604, AI085318, AA028905, AI809343, AA927327, AA621660, H18963,
					W79859, and U87223.
HSWAS18	1979	666302	1 - 481	15 - 495	AI341837, H29745, AI744756, R86286, H27353, and C02105.
HSWAR63	1980	471236	1 - 343	15-357	Al368388, Al375597, Al333175, Al096336, Al143097, Al371774, Al863007, Al143646,
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					Alo89622, Al807536, Al889890, Al283822, Al984147, Al436614, Al831700, Al401294,

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					AW303777, AW027683, AW70502, ALZ63596, AUZ6021, AU70054, AL160352, AL356262, AW306377, AW027683, AU70601, AL760565, AW138762, AW205241, AW131274, AW106777, AL263536, AW706762,
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$\dashv$	1881	697856	1 - 405	15 - 419	Al621111.
-	1982	936026	1-611	15 - 625	AA197067.
HPWSA52 1	1983	727294	1 - 336	15 - 350	H87580, and AL035699.

HPWDK45	1984	839559	1 - 521	15 - 535	R05355.
HPWDF03	1985	924978	1 - 701	15 - 715	W87370, AI168586, AA678331, T96677, W87371, and T96792.
HPWDE86	1986	785710	1 - 362	15 - 376	R34114, and R62645.
HPWCJ90	1987	789170	1 - 385	15 - 399	AA036882, AW001022, AI147683, AA046259, AI598152, AI201784, AW235719, AI696115,
3000	000,		,		and AAU 1 009.
HPWCG85	1988	638155	1 - 1025	15 - 1039	AW172969, AA601278, AA469230, AI376239, AI609972, AA847704, AI431434, AI249365,
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	15 - 233	15 - 546	15 - 291	15 - 340	15-216	15 - 565	15 - 497	15 - 592
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	1989	_	1991	1992	1993	1994	1995	+-
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HPRBN23	2015	467480	1 - 442	15 - 456	
HPRBI87	2016	695116	1 - 229	15 - 243	AA148577, AA371499, AI190166, AW182200, AW450886, and AL080125.
HPRBH80	2017	781636	1 - 395	15 - 409	AA371425, R08248, W78735, AA002229, AI034386, and AC004582.
HPRAV80	2018	781637	1 - 574	15 - 588	AI796794, H16396, AW450892, H06067, AA885838, AA370953, R40187, Z38928, F01486,
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HPRAN56	2019	503140	1 - 455	15 - 469	W55957, AI379296, AI191798, AA987330, AI688094, AA001362, AI655136, AI277583,
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HPRAN50	2020	724753	1 - 334	15 - 348	AA370553, and AA370552.
HPRAJ75	2021	766496	1-351	15 - 365	AA370391.
HPRAG73	2022	764757	1 - 734	15 - 748	W94997, AA370226, and AF123462.
HPRAG45	2023	484691	1 - 268	15 - 282	AA370201, AL031295, AL096775, AL034548, AL022323, AL049757, AL117258, AL021707.
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HPMSH94	2026	796839	1 - 599	15 - 613	AA214535.
HPMSB35	2027	_	1 - 245	15 - 259	W05600, and U47671.
HPMMK05	2028	-	1 - 824	15 - 838	AI312886, AA709064, R25113, R25114, AI271454, and AW131860.
HPMMB08	2029	957945	1 - 679	15 - 693	N57273, AA975894, AA078184, AW271847, AI720195, C13996, R67746, AI469577,
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HPMKC05	2031	930874	1 - 501	15-515	R97706, and Z73979.
HPMJT12	2032	969483	1 - 663	15 - 677	T84974, T91224, R00550, and R00654.
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HPMGD63	2044	694518	1 - 682	15 - 696	N59650, Z40592, F02367, and AA480778.
HPMFX29	2045	690704	1 - 616	15 - 630	W84490, W84350, AL044564, AI972017, AF086479, AF097027, AF097026, and AC002992.
HPMFL73	2046	867670	1 - 717	15 - 731	AA773011, and AF047825.
HPMFC02	2047	920327	1 - 904	15-918	AI361020, AI806300, AI339924, AA972324, AI689765, AI141310, AI798724, AI005122,
					AW015619, AI002107, AA721275, and Z59058.
HPMFB26	2048	867674	1 - 348	15 - 362	AA736385, AA262258, AL022164, AC005520, and AC007559.
HPMEG77	2049	772503	1 - 397	15-411	AA178897, AA178882, and AA179898.
HPMDQ89	2050	880787	1 - 444	15 - 458	AI634152, AI624814, AL135959, and AL049631.
HPMDP10	2051	968350	1-415	15 - 429	AW002399, AW450136, AI624994, AW082789, AI936619, AI953139, AA923323, AI377859.
					AI808017, AW452164, and AL109754.
HPMDF06	2052	954567	1 - 114	15 - 128	W28809.
HPMAM93	2053	791407	1 - 361	15 - 375	R42698, AI921147, AW001714, AA985608, AW025311, AI367373, and AA369641.
HPMAL77	2054	772740	1 - 628	15 - 642	AA149508, H66540, H53279, R99964, and AA369352.
HPMAL73	2055	764752	1 - 155	15 - 169	AA369348, AA018792, and AI439103.
HPMAK71	2056	203690	1 - 428	15 - 442	AA369278, AA369277, AA368633, AA297498, R86114, R92608, AC008101, AC016830.
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					AC004477, AC002369, AL035420, AC004916, AC005666, AC007371, AF111168, and
					AC007216.
HPMAJ83	2057	781518	1 - 396	15-410	R10536, and AA369467.
HPMAI80	2058	572808	1 - 331	15 - 345	AA369413.

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	15 - 450	15 - 552	 			15 - 285	15-515	15 - 538	15 - 450	15 - 560	15 - 222	15 - 366	15 - 327	15 - 747	15 - 514		15 - 495	15 - 576	15 - 608	15 - 529	15 - 373
	1 - 436	1 - 578				1-271	1 - 501	1 - 524	1 - 436	1 - 546	1 - 208	1 - 352	1-313	1 - 733	1 - 500		1 - 481	1 - 562	1 - 594	1 - 515	1 - 359
	783344	968723				679217	921331	731065	728517	712707	690962	787208	781854	9/547/	727885		/15/32	968707	963322	929723	928408
	2060	2062				2063	2064	2065	2066	2067	2068	2069	2070	707	2072	202	20/3	2074	2075	2076	2077
	HPMAH85	HPMAB10		-		HPLBW22	HPLBW02	HPLBT54	HPLBT53	HPLBS41	HPLBQ96	HPLB090	HPLBN79	HPLBB4/	HPLAX14	The Assessment	HFLA V44	HPLAI10	HPJFA10	HPJEV95	HPJEU01

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	AI085719, AA486414, AI270117, AI962050, AA652057, AI801600, AA771811, AI708009,
-	AI732186, AW303876, AW162049, AI929531, AA598586, AI610159, AA713815, AW265009,
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HPJCT26	2090	559949	1 - 628	15 - 642	
HPJCS73	2091	975087	1 - 540	15 - 554	AC009533, and AC008013.
HPJCS43	2092	715082	1 - 426	15 - 440	
HPJCS32	2093	699046	1 - 261	15 - 275	
HPJCN60	2094	887600	1 - 408	15 - 422	AC005754, and AF152495.
HPJCL55	2095	670083	1 - 580	15 - 594	AA460600, AA971933, AA461528, AI028767, AW104221, AA916255, AI807812, AA815321
					AA609716, AA897273, and AA382975.
HPJBU40	2096	710928	1-411	15 - 425	T79399, T79485, and AC004460.
HPJBU09	2097	625362	1 - 520	15 - 534	H14685, H11846, and Z42042.
HPJBS74	2098	765390	1 - 579	15 - 593	AA199800.
HPJBS52	2099	726535	1 - 505	15 - 519	R69458.

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R08072.	N20501, W21595, AA971971, A1017087, AA782105, A1924135, and AC007066	AI743553, AI458005, AA855142, AI808388, AI808190, AA854848, AI167631, AI458852, AI740975, AI184926, AI027358, AI084343, AI041477, AA860979, AA782086, AI864309, AA585255, and AI 035562	170000000000000000000000000000000000000	Z98272, and AC005202	H02676, R21208, and AC006480.		W04456, H09371, D59238, H09370, N34243, AA091691, and N75681	Z97832.	A1284640, A1801600, AA745582, AA491814, A1350211, AA745431. A1902694, AW080134	AI053672, AL133723, AW193265, AI688846, AI446464, AA492132, AA985038, AA747480	AA350859, AA318652, AI286356, AI471543, AI679045, AA649642, AI610159, AA503558	H64777, AA515435, AI761471, AI469624, T07451, AI281697, AI251002, AI205126, F75776	AA977743, AA515751, AA559290, AI281881, AW419262, AI610376, AW276435, AA678436	AA747276, AW088058, AW274349, AI648558, F29989, AI061334, AA605774, AA747477	F36273, AI962050, AI287651, AA553465, AI264743, AI34844, AI198376, AA377730.	AA483034, AA650244, AA469451, AI312149, AI049634, AA745560, AI918421, AI471481.	AW103981, AI937850, AA490165, AI768952, AA659083, AI367975, AA594145, F18974.	AI245679, AA364224, AA365302, AA680243, AI286264, AI624698, AW440976, AA441788.	T40338, AW236342, AA521323, AA557879, AA843450, AW265170, AI287964, AW029038.	AL046409, F31204, F28776, F37169, H64560, AI305547, AW193432, AI339850, AI963720.	T53607, AI929531, AL120483, AA347927, AA708678, AI282832, AI358571, R91994,	AI904894, AW243960, AI358343, AW243698, AI184226, AW166815, AA657918, AA515051,	F23279, AL045182, AI355206, AW264973, AI919029, AI431303, F33566, AW276827,	AA347930, F37286, AW303196, AA886584, AA244415, AI206785, N43757, AA302963,	AA482711, AA338486, AI270117, AA501722, AA229785, AI821271, AA503154, AA669840,	F35673, AA557686, AI653905, N71930, AW272758, AW301350, AA358122, AA654771,	F34558, AW104748, AW406755, AA664535, AA100372, AA084070, AA810318, AW265654,	AA364456, AI924251, AW261871, AA682912, AW088202, H41319, T08638, AI619997,	AW162049, AI832782, AI633007, Z98473, AA581903, AI358501, AA669251, AA394271,	A1365988, A1569086, F28576, A1083946, A1963095, AA610491, A1866956, A1299050, F28204,	100/83, A W 2382/8, Al692265, Al802526, Al358229, AA515224, T40617, T29180, Al083998,	AL119691, AA528516, AI309740, T40077, F26152, C75026, AI709365, AI133636, AI081095,	AF130152, AA715609, AI567674, AC004076, AF019664, D83989, X75335, AC007446.
15 - 441	15 - 778	15 - 1128	15-213	15 - 331	15 - 405	15 - 762	15 - 320	15 - 430	15 - 909																								
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2100	2101	2102	2103	2104	2105	2106	2107	2108	2109																					-			
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	1 - 348	1 - 434	1 - 804	1 - 504	1 - 475	1 - 459	1 - 426	1 - 428								1 - 426			1 - 165	1 - 234	1 - 172	1 - 405	1 - 713		1 - 373							
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	HPFDX38	HPFCZ82	HPFCZ60	HPFCZ10	HPFCR23	HPFCP82

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961865     1 - 595     15 - 609       933737     1 - 324     15 - 338       926209     1 - 165     15 - 179       909030     1 - 432     15 - 446       948619     1 - 514     15 - 528					AF119337, A93350, 126207, 166342, AF026816, AI.137576, AC003940, E15569, AL133077,
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	HOVDD10	HOVCP77	HOVCO50	HOVCN57	HOVCM77	HOVCM03	HOVCI89	HOVCI08		HOVCD33	HOVCC57	HOVBQ07	HOVBK69	HOVBK38				HOVBK24	HOVBI67	HOVB120	HOVAZ89	HOVAZ65	HOVAY88	HOVAY58

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	15 - 408	15 - 686	15 - 493	15 - 591		15 - 359	15 - 555	15 - 486	15 - 252	15 - 386	15 - 444	15-437	15 - 429	15 - 809					0,0	15 - 249	15 - 556		
	1 - 394	1 - 672	1 - 479	1-577		1 - 345	1 - 541	1 - 472	1 - 238	1 - 372	1 - 430	1 - 423	1 - 415	1 - 795					225	1 - 233	1 - 542		
	578788	578791	961499	925784		925774	925783	965292	-	_	928644	922510	917424	969061			-		033033	+	177776		
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	HOVAB85	HOVAB61	HOOKF10	HOOKF04		H00J004	HOOJN04	HOOJK11	ноолн05	HOOJE02	HOOIL05	HOOIG03	НООНР02	НООНЕ67					HOODING	HOOLDOO	HOGAB23		

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					ALI049/09, AI4/1481, AW193265, AI963720, AI560085, AL079869, AI287651, AL046409,
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2272     745130     1-430     15-444       2273     750308     1-547     15-561       2274     847191     1-394     15-408       2275     682232     1-281     15-295       2276     908904     1-960     15-974	
2273     750308     1 - 547     15 - 561       2274     847191     1 - 394     15 - 408       2275     682232     1 - 281     15 - 295       2276     908904     1 - 960     15 - 974	15 - 444 AA021008, and AA057308.
2274     847191     1 - 394     15 - 408       2275     682232     1 - 281     15 - 295       2276     908904     1 - 960     15 - 974	15 - 561 T97004, AI076315, and T87200.
2275 682232 1-281 15-295 2276 908904 1-960 15-974	15 - 408 AA923566, AI754510, AI018234, W68384, AI376764, AI335263, AI769932, AI143581, AA456821, AI949857, W18181, AW305247, AI613113, W68500, H30442, AI190109, H11954, R44819, AA873841, AA767140, R16196, H30441, R16198, T16809, and H82480
2276   908904   1 - 960   15 - 974	
11/ 61	15 - 974 AI631040, and AA594778.
2277 764490 1 - 412 15 - 426	15 - 426 AA258075, AC007688, AC004878, AL133500, and AC006241.
2278 681919 1 - 497 15 - 511	
2279 760431 1 - 355 15 - 369	
HOGAG57 2280 734848 1 - 621 15 - 635 AA737314, AA683 AA188649, and A	15 - 635 AA737314, AA682280, AA010792, AA143573, AA953433, H23757, AA011221, AA745273, AA188649, and AF205935.

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1 - 563	1 - 694											1 - 499		1 - 658				1 - 142	1-417	107	1 - 397	1 - 465	1 - 366	1 - 353	1 - 303	1 - 332	1 - 353	1 - 337	1 - 396	1 - 290	1 - 346
772319	756713				-							789232		533713	•			753048	815822	720755	953436	724437	888569	788947	784366	760643	760392	859094	859093	713816	859102
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HOGAD77	HOGAC69											HOFNW81		HOFNW69				HOFNW68	HOFNW65	HOFNW45	HOFNW07	HOFNU50	HOFNL96	HOFNI90	HOFN185	HOFNI72	HOFNI71	HOFNI58	HOFNIS6	HOFNI42	HOFNI37

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AW248328.		D86969, AF127774, and Z83822.				AI251832, AA622670, AA888154, AA994676, AA890531, A1141391, A1025322, A1587539	AA628616, AI338781, AW055053, AI147905, AA040767, AW272916, AI192845, AI338006	AI095692, AI144012, AI051360, AI205873, AA970491, AI374939, AI678799, AI869782.	AI423147, AA973818, AI439825, AI520772, AW438950, AI694600, AI040992, AA935932,	AA418706, AI091801, AI750219, AA425949, AI636432, AI079960, AA872649, AI061431	AA779735, AW275907, AA576868, H97795, W61292, AA814520, AW440409, AA812517,	AI274100, AI128370, AA861315, AW169816, AA026344, N50703, AW440389, AA147089.	AI887699, H25461, AW270131, AI201428, AA099879, A1080203, AA173333, AA147095	Z21890, AW023278, AA780492, R52994, AI630374, AA173438, AW189739, AI890908.	AA714013, R31084, H28954, AA037330, AA468886, T06660, AI217891, H07854, AA176908	241333, AI949085, D57501, AI351274, AA037329, AI864848, R34332, AA885673, AI079089	R80423, AA599378, AA464883, AI784205, R41882, AI864749, AI860102, T04889, T15425	AW189623, AA418715, AI982539, D53365, AW237884 T35361 AA784089 T25643	AA629755, W52902, H27251, AA489825, AI718058, AF000987, and 1142186				AI394585, AI347406, AW300884, R60771, AI609950, N94357, AA768117, AA830837	AA778534, AI024114, AJ340016, AI675916, AW027671, AW027648. AA983621. AJ272784	AA918495, AA724472, AI335706, AI421130, AI340312, AI632085, AI159997, F35349.	R49581, W52231, R36293, AL119324, AI431351, AL119399, AL119464. AI432666, AI 119457	AI431346, AI432662, AI431243, AL042544, AI623302, AW392670, AI431354, AI431307	AI431316, AW372827, AL119443, AI432644, AI432649, AI431337, AI431312, AI432674	AL119355, AW128897, AI791349, U46351, AI432651, AI431230, Z99396, AI492509, U46350.	AI432661, AL119319, AL134902, AI431238, U46349, AW081103, AI432675, AI431347.	AI432653, AL119483, AI431328, AI432654, AI432655, AI431310, AW384394, AI432650.	AI432677, AW363220, AL119497, AI432665, AL119484, AL119363, AL119391, AI431248	A1431330, U46347, A1432647, A1492519, U46341, AL119444, AL119401, A1432657,	AL119341, AI431241, AI431345, AW128900, AL119418, AL042450, AI432643, AI431353,	A1492510, A1431247, AL119439, A1431357, AL119522, AL119396, U46346, AL119335,
15 - 347	15 - 378	15-319	15 - 203	15 - 367	15 - 425	15 - 321														15 - 68	15 - 433	15 - 156	15 - 1359												
1 - 333	1 - 364	1 - 305	1 - 189	1 - 353	1 - 411	1 - 307														1 - 54	1 - 419	1 - 142	1 - 1345												
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2299	2300	2301	2302	2303	2304	2305														2306	2307	2308	2309												
HOFNI33	HOFNI32	HOFNI10	HOFNI02	HOFNC80	HOFNC79	HOFNB63														HOFNB55	HOFNB51	HOFMU70	HOFMU67												

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HODCY73	2359	764543	1 - 447	15 - 461	AI816780, AI458427, AI828772, AA970754, T90292. AA723211. C15270. R55335. A1700847
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TO CONTINUE OF	7047	977076	C+/ - 1	6C/ - CI	AA814415, A1378392, N45120, A1457108, AA809495, AA835661, AA831169, A1351546, R43018 R44581 A1824326 and AW126237
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_	15 - 497	AA954976, AI017449, T89711, W69257, AI150048, AA534436, T89631, AI261657,
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HLWAS09	2447	625419	1 - 223	15-237	AA602628, AA352444, AA363279, AC005969, AC004087, AL035414, AC006511, AL109627,
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HLWAL31	2450	948928	1 - 110	15 - 124	
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HLWAF02	2452	919714	1 - 1216	15 - 1230	AW003851, AW088297, AI004165, AW269624, AW073468, AA577265, W72446, AI863050
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HLWAD33	2455	-	1 - 454	15 - 468	AI220952, R21518, AC004675, and AF088219.
HLWAD32	2456	-	1 - 289	15 - 303	
HLWAD02	2457	919725	1 - 529	15 - 543	AI500547, and AW276592.
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НЕОАА93	2501	792255	1 - 546	15 - 560	W92197, A1272825, AA016235, W94926, A1243425, AW082258, AW297127, A1241137, A1424820, AA813649, and A1289258.
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HEPBO92	2503	952996	1 - 427	15-441	W80428, AI281960, W58699, AA417821, AI191334, AA524259, AI140335, AI272028.
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HEPAN05	2510	932893	1 - 477	15 - 491	AI218711, AI918047, AI918977, AI288674, AI085618, AI139776, F29008, AA335421.
					AI929165, F35667, AC004751, and AC004646.
HEPAK04	2511	933039	1 - 477	15 - 491	AI004158, AA335529, AA847893, AI262232, AW292700, AI950883, AA808598, AW183055

AA505961, AA478576, AA255751, AI468599, AI417159, AI678423, AW043579, AI333775, AI521274, AA009947, AI379044, AI089360, AI027938, AW173026, N49409, AA417796, AA173415, R94723, AI972464, W31503, H63962, AI703182, AW193647, AI741193, AA456887, AA470626, AA886885, D130022, AM1966657	H26683, and AA335271,	AI219496, AI187819, AW085963, AA335263, AA669515, AC007003, and A C007004	R46509, AA335475, AA335926, and Z63111.	AA484651, AA335440, and AC004887.	AI445299, AW005649, AI470184. AB032959. and AI 021393	AW295266, AI765278, AI261553, AI367242, AI050799, AI433693, AI672068, AI308137	A1769877, AW003759, AI201838, H18343, AI761277, AI823875, R85423, H18100, A1760769	AI984928, AW149699, H20325, R84272, AA860751, AI369859, AI262936, AI474901,	AA013231, AA013325, and H18141.	T51466, and AC006333.	AA236038.	H54234, AL037663, W84821, AJ012221, A1007014, and A1031219	AI962879, AA133284, AI863307, AI679213, AA768727 AA417760 AI083774 HOSGOO	AI538225, AW409962, AA516124, AA417846, AW196578, AW074110, AI168476, AI825102	and AI885413.	AA059456, AA040649, R60003, AA058951, AI970861, AA662962, AW268083, and	AA045527.	AA813370, and Z93016.	N77524.	AW305246, AA405462, and AA336099.	AA176878, AA984649, and AB009973.	AA083887.	AA086139, AI088145, AW131790, AI857700, AI283095, AI813629, AI917113, AI478664	AI919281, AI967944, AI499083, AI655215, AW136596, AI767765, AI825582. W16832.	AA831238, AI381212, AW028578, Z19309, AA912593. A1497888 H86248 AA019370 and	AF061261.	AI832117, and T60136.	T90469.	AA158378.	W94212.	T51329, R55106, AW298352, U73637, AF015416, and AF083108.
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7	2550	951655	1 - 476	15 - 490	AI027619, AA926665, AA954546, AA398085, AA621275, AA634531, and AA724256
┪	2551	951693	1 - 504	15 - 518	AI160370, AA993156, and AW269609.
-	2552	917577	1 - 332	15 - 346	AA226397, H29285, Z39193, and D61466.
HCONM33	2553	971637	1 - 463	15 - 477	A1339840, N40932, AW044507, AI216527, AI620878, AW316937, AI292180, AI358083
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	1 - 438	1 - 474	1 - 678	
	754392	773043	880276	
	2625	2626	2627	
	HBGMS69	HBGMO78	HBGMG81	

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				2631 861602
·		$\dashv$	HBGDH33 26	HBGDF39 26

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1 - 474	1 - 43	1 - 192	1 - 245	1-137	1 - 94
832888	802090	588263	522424	525837	971466
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HBGDA74	HBGBG69	HBGBG67	HBGBG52	HBGBG38	HBGBE12

HBGBB78	2638	773930	1 - 329	15 - 343	H51141, and D37934.
HBCPV80	2639	932817	1 - 390	15 - 404	Al306162, AI492835, AC002359, and AC002365.
HBCP075	2640	927520	1 - 473	15 - 487	AI017490, AI221329, AA973064, AA813611, AI688144, AI222206, AW182987, AA883877, W31185, AI208514, AI917508, and AI810095.
HBCPK03	2641	922493	1 - 720	15 - 734	AA831288.
HBCJP02	2642	186216	1 - 494	15 - 508	A1188098, AW304309, AI375434, AI625524, AI016723, AI167974, AI302664, AW001092, AI246687, AI572643, AI201622, AW151711, AW167729, AI609516, AI687735, AI191064, AI289182, AI191358, AI024836, AA6323308, AI831665, AI084459, AI088372, A A 2 4 8 1 8 1 8 1 8 1 8 1 8 1 8 1 8 1 8 1 8
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HBCJG07	2643	951898	1 - 375	15 - 389	R82747, R30969, and T87286.
HAUCC58	2644	764851	1 - 390	15 - 404	AA235095, W63805, W07740, AA302624, AA293831, AA315199, R53208, AI568567,
					AI992241, AI086596, AW151172, AA309877, AI080304, AA401651, AW090277, AA150647,
					AA708776, AA142944, AI826693, AA843315, N77987, AW051448, AA527053, N92512, R87425, A1120510, A12088, A1082531, A1235805, A1020605, A120810, A12081
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					AI074899, AI193867, AA249309, F32557, AA722032, N80680, W38964, F24549, T83037,
					AA402479, AA844466, AI141356, N58395, AA454862, AI161139, AW008542, W93969,
					W93970, AA336147, R48412, AI378335, T90357, H95941, AA568295, R86694, AA341105,
					AA228455, AW352337, W30921, AW337638, N74117, AA303783, AA215973, AW009811,
					R53110, AA558040, AI961636, F24945, AA715148, R49774, F35088, AA228454, AA328964,
					AAU//962, K11503, H8/636, A1695590, AA904185, AA398459, A1803601, R86695,
HAUAW51	2645	577959	1 - 336	15-350	AA214667 and H78996
HAUAS89	2646	518847	1 - 164	15-178	AA926970, F27522, F30071, AA096277, AA627396, F33364, AA318284, AI283651, F77676
					AW015956, AA947143, AA244132, AA327732, AA352731, AA320725, AA089891, AA317435,
					AA319168, F30100, AA664996, F29754, F27644, F27760, AI832645, F24555, AIS60279,
					AA306681, AI749712, AI289147, AI130748, AA694164, AI023676, AA244131, F26815,
					AI039009, F33405, AI309287, AA534561, T74859, F35771, F34894, F35313, W78719, F30920,
					AA694524, AA524049, AI150756, AI344732, D51606, AA903996, AA864997, AC008044, and
HAIIAO28	2647	685374	1 520	15 534	71.000007 Z.
120114	2011	110000	1 - 360	10 - 004	AA12/394;

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15 - 527	15 - 453	15 - 499
1 - 513	1 - 439	1 - 485
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2648	2649	2650
HAQCF25	HAQCD07	HACMR08

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-	AC004448, AC007073, AL033525, AC005255, AC004890, AC005324, AC005578, AL031005.
	AC007225, AF111168, AC005726, AC005821, AL035587, AC005207, AC004408, AL022327.
	AC005529, U95742, AC006026, AC004136, AC004150, AC005736, AC007052, AF134726.
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	AC016831, AC008115, AF146191, AC004659, AL035405, AL021393, AC005899, AC002365.
	AF001549, AC006101, AL021546, AL117344, Z97056, AL133246, AL034548, Y18000.
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	AP000505, AC005874, AF134471, AC004796, AL031117, AL109627, AL049643, AL049748.
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	Y10196, AC005520, AC005057, AF064861, AL049843, AC005102, AC004812, AC002418.
	AC005295, AC002553, AL110502, AF190465, AL121603, AC000385, AC007546, AL022162.
	AC005730, AC005484, AC004887, AC004000, AL122023, AC005280, AC003043, AC002504.
	AL031295, AC007537, Z68269, AF015148, AC008044, AB026898, AL109628, and AI420248.

## TABLE 4

AR022   a Heart	Code	Description	Tiene	Το	1600		
AR023			Tissue	Organ	Cell Line	Disease	Vector
AR024				<del> </del>			
AR025   A Prostate   a Frostate   a Stomach   AR027   a Stomach   a Stomach   a Stomach   AR028   Blood B cells   Blood B cells   Blood B cells   AR029   Blood B cells   Blood B cells   Call   Blood B cells   Call   C				<del> </del>	<del></del>		
AR026   a small intestine   a small intestine   AR027   a Stomach   AR028   Blood B cells   Blood B cells   Blood B cells   Call   Blood B cells   Call   Blood B cells   Call				<del>                                      </del>	<del></del>		ļ <u></u>
AR027   a Stormach   a Stormach   AR028   Blood B cells   Blood B cells   activated   Blood B cells   activated   Blood B cells   activated   Blood B cells   activated   Blood B cells   activated   Blood B cells   activated   Blood C cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated   Blood T cells   activated		<del></del>		<del> </del>			
AR028   Blood B cells   Blood B cells					<del></del>		<del> </del>
AR029   Blood B cells activated   Blood B cells   activated   Blood B cells   resting   Blood B cells   resting   Blood T cells   activated   activated   activa							<del> </del>
AR030   Blood B cells resting   Blood T cells activated   AR031   Blood T cells activated   AR032   Blood T cells resting   Blood T cells resting   AR033   Blood T cells resting   Blood T cells resting   AR033   Drain					<del></del>		<del> </del>
AR030   Blood B cells resting   Blood B cells   resting   resting   R031   Blood T cells activated   Blood T cells   activated   AR032   Blood T cells resting   Blood T cells resting   Blood T cells resting   AR033   Darian							
RR031   Blood T cells activated   Blood T cells   RR032   Blood T cells resting   Blood T cells resting   Blood T cells resting   Blood T cells resting   RR033   Drain   Dr	AR030	Blood B cells resting		<del> </del>			<del> </del>
AR031   Blood T cells activated   Blood T cells   AR032   Blood T cells resting   Blood T cells resting   Blood T cells resting   AR033   brain   brain   brain   brain   AR034   breast   breast   breast   AR035   breast cancer   cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line PA-1   cell line PA-1   cell line PA-1   cell line PA-1   cell line PA-1   cell line PA-1   colon (9808co58R)   colon   Colon   Colon   Colon   Colon (9808co58R)   colon (9809co15)   colon (9809co15)   colon (9809co15)   colon (9809co15)   colon (9809co15)   Colon (9809co15)   colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co14)   Colon cancer   Colon							
AR032   Blood T cells resting   Blood T cells resting   Drain	AR031	Blood T cells activated					<del> </del>
AR033   brain   brain   brain   brain   AR034   breast   breast   breast   ancer   breast cancer   AR036   Cell Line CAOV3   Cell CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell CAOV3   Cell Line CAOV3   Cell CAOV3   Cell Line CAOV3   Cell CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line				i			1
AR033   brain   brain   brain   AR034   breast   breast   breast   AR035   breast cancer   breast cancer   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line PA-1   Cell line PA-1   Cell line PA-1   Cell line PA-1   Cell line PA-1   Cell line PA-1   Cell line transformed   Cell line transformed   Cell line transformed   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell CAOV		Blood T cells resting	Blood T cells resting			<del></del>	<del> </del>
AR035 breast cancer breast cancer   AR036 Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line CAOV3   Cell Line transformed   Cell line transformed   Cell line transformed   Cell Line transformed   Cell Line CAOV3   Cell Line CAOV3   Cell Line transformed   Cell Line transformed   Cell Line transformed   Cell Line CAOV3   Cell Line CAOV3   Cell CANOV3   Ce	AR033	brain					<u> </u>
AR036   Cell Line CAOV3   Cell Line CAOV3   AR037   cell Line PA-1   cell Line PA-1   cell Line PA-1   AR038   cell Line transformed   cell Line transformed   Cell Line tra		breast	breast			<del>'</del>	<del> </del>
AR037   Cell line PA-1   Cell line PA-1   Cell line PA-1   Cell line transformed   Cell line transfo			breast cancer				
AR038   Cell line transformed   Cell line transformed   AR039   Colon   Colo			Cell Line CAOV3				
AR039   Colon   Colon   Colon   AR040   Colon   (9808co65R)   Colon   (9808co65R)   Colon   (9809co15)   Colon   (9809co15)   Colon   (9809co15)   Colon   (9809co15)   Colon   (9809co15)   Colon   (9809co15)   Colon   (9809co15)   Colon   (9808co64R)   Colon cancer   Colon cancer   (9808co64R)   Colon cancer   (9808co64R)   Colon cancer   (9808co64R)   Colon cancer   (9808co64R)   Colon cancer   (9808co64R)   Colon cancer   (9808co64R)   Colon   Co			cell line PA-1			<del></del>	
AR040   Colon (9808co65R)   Colon (9808co65R)   AR041   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon (9809co15)   Colon cancer   Colon canc	AR038	cell line transformed	cell line transformed		·		
AR041   colon (9809co15)   colon (9809co15)			colon				
AR041   colon (9809co15)   colon (9809co15)	AR040	colon (9808co65R)	colon (9808co65R)	· · · · · · · · · · · · · · · · · · ·			
AR043   Colon cancer (9808co64R)   Colon cancer (9808co64R)     AR044   Colon cancer 9809co14   Colon cancer 9809co14     AR045   Corm clone 5   Corm clone 5     AR046   Corm clone 6   Corm clone 6     AR047   Corm clone2   Corm clone3     AR048   Corm clone4   Corm clone4     AR050   Donor II B Cells 24hrs   Donor II B Cells 24hrs     AR051   Donor II B-Cells 72hrs   Donor II B-Cells 24hrs     AR052   Donor II B-Cells 72hrs   Donor II B-Cells 24hrs     AR053   Donor II B-Cells 72hrs   Donor II B-Cells 72hrs     AR054   Donor II Resting B Cells   Donor II Resting B Cells     AR055   Heart   Heart     AR056   Human Lung (clonetech)   Human Lung (clonetech)     AR057   Human Mammary   Human Mammary (clonetech)     AR058   Human Thymus   Human Mammary (clonetech)     AR059   Jurkat (unstimulated)   Jurkat (unstimulated)     AR050   Kidney   Kidney     AR060   Kidney   Kidney     AR061   Liver   Liver     AR063   Lymphocytes chronic   Lymphocytes     AR063   Lymphocytes chronic   Lymphocytes     AR064   Liver (Clontech)     AR065   Liver (Clontech)   Liver (Clontech)     AR066   Liver (Clontech)   Liver (Clontech)     AR066   Liver (Clontech)   Liver (Clontech)     AR066   Liver (Clontech)   Liver (Clontech)     AR067   Liver (Liv		colon (9809co15)	colon (9809co15)		<del></del>		<del>                                     </del>
AR044   Colon cancer 9809co14   Colon cancer 9809co14   Colon cancer 9809co14   AR045   Corn clone 5   Corn clone 5   Corn clone 6   Corn c			colon cancer				
AR044 colon cancer 9809co14 colon cancer 9809co14  AR045 com clone 5 com clone 6 com clone 6  AR046 com clone 6 com clone 2  AR047 com clone2 com clone2  AR048 com clone3 com clone3  AR049 Com Clone4 Com Clone4  AR050 Donor II B Cells 24hrs Donor II B Cells 24hrs  AR051 Donor II B Cells 72hrs Donor II B Cells 72hrs  AR052 Donor II B-Cells 24 hrs. Donor II B-Cells 24 hrs.  AR053 Donor II B-Cells 72hrs Donor II B-Cells 72hrs  AR054 Donor II Resting B Cells Cells Tel	AR043	colon cancer (9808co64R)	colon cancer		1		<del></del>
AR045 corn clone 5 corn clone 5 AR046 corn clone 6 corn clone 6 AR047 corn clone2 corn clone2 AR048 corn clone3 corn clone3 AR049 Corn Clone4 AR050 Donor II B Cells 24hrs Donor II B Cells 24hrs  AR051 Donor II B-Cells 72hrs Donor II B Cells 72hrs  AR052 Donor II B-Cells 24 hrs. brs. AR053 Donor II B-Cells 72hrs Donor II B-Cells 72hrs AR054 Donor II Resting B Cells Cells AR055 Heart Heart Heart AR056 Human Lung (clonetech) AR057 Human Mammary (clontech) AR058 Human Thymus (clonetech) AR058 Human Thymus (clonetech) AR059 Jurkat (unstimulated) AR050 Kidney AR061 Liver (Clontech) AR061 Liver (Clontech) AR062 Liver (Clontech) AR063 Lymphocytes chronic Liver (Clontech) AR063 Lymphocytes  Liver (Clontech) AR063 Lymphocytes  Corn clone 5 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 5 Corn clone 5 Corn clone 5 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 6 Corn clone 5 Corn clone 5 Corn clone 5 Corn clone 5 Corn clone 6 Corn clone 6 Corn clone 5 Corn clone 1 Corn clone 4 Corn Clone 6 Corn clone 1 Corn c			(9808co64R)		1 1		
AR045         com clone 5         com clone 6           AR046         com clone 6         com clone 6           AR047         com clone2         com clone2           AR048         com clone3         com clone3           AR049         Com Clone4         Com Clone4           AR050         Donor II B Cells 24hrs         Donor II B Cells           AR051         Donor II B Cells 72hrs         Donor II B Cells           72hrs         Donor II B-Cells 24 hrs.         Donor II B-Cells 24 hrs.           AR052         Donor II B-Cells 72hrs         Donor II B-Cells 24 hrs.           AR053         Donor II Resting B Cells         Cells           AR054         Donor II Resting B Cells         Cells           AR055         Heart         Heart         Heart           AR056         Human Lung (clonetech)         (clonetech)         Human Lung           (clonetech)         (clonetech)         (clonetech)           AR057         Human Mammary         (clonetech)         (clonetech)           AR058         Human Thymus         (clonetech)         (clonetech)           AR059         Jurkat (unstimulated)         Jurkat (unstimulated)         Jurkat (unstimulated)           AR061         Liver         Liver (Clon	AR044	colon cancer 9809co14	colon cancer				
AR046   corn clone 6   corn clone 6   AR047   corn clone 2   corn clone 2   corn clone 2   AR048   corn clone 3   corn clone 4   AR049   Corn Clone 4   Corn Clone 4   AR050   Donor II B Cells 24hrs   Donor II B Cells 24hrs   AR051   Donor II B Cells 72hrs   Donor II B Cells 24hrs   AR052   Donor II B-Cells 24 hrs.   Donor II B-Cells 24 hrs.   AR053   Donor II B-Cells 72hrs   Donor II B-Cells 72hrs   Donor II B-Cells 72hrs   AR054   Donor II Resting B Cells   Donor II Resting B Cells   AR055   Heart   Heart   Heart   Heart   AR056   Human Lung (clonetech)   Human Lung (clonetech)   (clonetech)   (clonetech)   AR057   Human Mammary   Human Mammary   (clonetech)   (clonetech)   Human Thymus   (clonetech)   AR058   Human Thymus   Human Thymus   (clonetech)   (clonetech)   AR059   Jurkat (unstimulated)   Jurkat (unstimulated)   Jurkat (unstimulated)   AR060   Kidney   Kidney   Kidney   Kidney   AR061   Liver   Liver (Clontech)   Liver (Clontech)   Lymphocytes   Lymphocytes   Liver (Clontech)   Lymphocytes   Liver (Liver (Liver)   Lymphocytes   Liver (Liver)	<u> </u>		9809co14		-		
AR047   corn clone2   corn clone2   AR048   corn clone3   corn clone3   Corn clone4   AR049   Corn Clone4   Corn Clone4   AR050   Donor II B Cells 24hrs   Donor II B Cells 24hrs   AR051   Donor II B Cells 72hrs   Donor II B Cells 24 hrs.   Donor II B-Cells 24 hrs.   Donor II B-Cells 24 hrs.   Donor II B-Cells 24 hrs.   Donor II B-Cells 72hrs   Donor II B-Cells 72hrs   Donor II B-Cells 72hrs   Donor II Resting B Cells   T2hrs   Donor II Resting B Cells   Ce			corn clone 5				
AR048   corn clone3   corn clone3   AR049   Corn Clone4   Corn Clone4   AR050   Donor II B Cells 24hrs   Donor II B Cells 24hrs   AR051   Donor II B Cells 24hrs   Donor II B Cells 24hrs   AR052   Donor II B-Cells 24 hrs.   Donor II B-Cells 24 hrs.   AR053   Donor II B-Cells 72hrs   Donor II B-Cells 24 hrs.   AR054   Donor II Resting B Cells   Donor II Resting B Cells   Cells			corn clone 6				
AR049   Corn Clone4   Corn Clone4			com clone2				
AR050 Donor II B Cells 24hrs  AR051 Donor II B Cells 72hrs  Donor II B Cells  72hrs  AR052 Donor II B-Cells 24 hrs.  AR053 Donor II B-Cells 72hrs  Donor II B-Cells 24  hrs.  AR054 Donor II Resting B Cells  Cells  AR055 Heart  AR056 Human Lung (clonetech)  AR057 Human Mammary (clontech)  AR058 Human Thymus (clonetech)  AR059 Jurkat (unstimulated)  AR050 Kidney  AR060 Kidney  AR061 Liver  AR060 Liver (Clontech)  AR060 Liver (Clontech)  AR060 Liver (Clontech)  AR060 Liver (Clontech)  AR060 Liver (Clontech)  Liver (Clontech)  AR060 Liver (Clontech)			corn clone3				
AR051   Donor II B Cells 72hrs   Donor II B Cells   72hrs							
AR051 Donor II B Cells 72hrs  AR052 Donor II B-Cells 24 hrs.  AR053 Donor II B-Cells 72hrs  AR054 Donor II Resting B Cells  AR055 Heart  AR056 Human Lung (clonetech)  AR057 Human Mammary (clontech)  AR058 Human Thymus (clonetech)  AR059 Jurkat (unstimulated)  AR059 Jurkat (unstimulated)  AR050 Kidney  AR060 Kidney  AR060 Liver (Clontech)	AR050	Donor II B Cells 24hrs					
AR052 Donor II B-Cells 24 hrs. Donor II B-Cells 24 hrs.  AR053 Donor II B-Cells 72hrs Donor II B-Cells 72hrs  AR054 Donor II Resting B Cells Cells Ponor II Resting B Cells Ponor II B-Cells 24 hrs.  AR055 Heart Ponor II B-Cells 24 hrs.  Heart Ponor II Resting B Cells Ponor II B-Cells						;	
AR052 Donor II B-Cells 24 hrs.  AR053 Donor II B-Cells 72hrs  AR054 Donor II Resting B Cells  AR055 Heart  AR056 Human Lung (clonetech)  AR057 Human Mammary (clonetech)  AR058 Human Thymus (clonetech)  AR059 Jurkat (unstimulated)  AR050 Kidney  AR060 Kidney  AR061 Liver  AR060 Liver (Clontech)  AR063 Lymphocytes chronic  Donor II B-Cells 24 hrs.  Donor II B-Cells 24 hrs.  Donor II B-Cells 24 hrs.  Donor II B-Cells 24 hrs.  Donor II B-Cells 24 hrs.  Liver (Clols  AR061 Liver (Clonetech)  Donor II B-Cells 24 hrs.  Human Tlance (Cells Human Lung (Cells Human Lung (Clonetech) (Cl	ARUSI	Donor II B Cells 72hrs					
AR053 Donor II B-Cells 72hrs Donor II B-Cells 72hrs  AR054 Donor II Resting B Cells Donor II Resting B Cells  AR055 Heart Heart  AR056 Human Lung (clonetech) AR057 Human Mammary (clontech)  AR058 Human Thymus (clonetech)  AR059 Jurkat (unstimulated)  AR059 Jurkat (unstimulated)  AR060 Kidney  AR061 Liver  AR062 Liver (Clontech)  Liver (Clontech)  AR063 Lymphocytes chronic  Donor II B-Cells 72hrs Donor II B-Cells 72hrs Colls Heart Heart Heart Human Lung (clonetech)  (clonetech)  Human Lung (clonetech)  (clonetech)  Aruman Thymus (clonetech)  Aruman Thymus (clonetech)  Liver Liver Liver Liver Liver (Clontech)  Aruman Lung (clonetech)  Lymphocytes	4 D 0 5 0	- "50"					
AR053 Donor II B-Cells 72hrs  AR054 Donor II Resting B Cells  AR055 Heart  AR056 Human Lung (clonetech)  AR057 Human Mammary (clontech)  AR058 Human Thymus (clonetech)  AR059 Jurkat (unstimulated)  AR060 Kidney  AR061 Liver  AR063 Lymphocytes chronic  Donor II B-Cells  72hrs  Donor II Resting B  Cells  Human Tlesting B  Cells  Human Lung (clone (clonetech)  Human Lung (clonetech)  Human Mammary (clonetech)  Human Mammary (clonetech)  Human Thymus (clonetech)  (clonetech)  AR060 Kidney  Kidney  AR061 Liver  Liver (Clontech)  AR063 Lymphocytes	ARU52	Donor II B-Cells 24 hrs.					
AR054 Donor II Resting B Cells Donor II Resting B Cells  AR055 Heart Heart  AR056 Human Lung (clonetech)  AR057 Human Mammary (clontech)  AR058 Human Thymus (clonetech)  (clonetech)  AR059 Jurkat (unstimulated)  AR060 Kidney  AR061 Liver  AR062 Liver (Clontech)  AR063 Lymphocytes chronic  Donor II Resting B  Donor II Resting B  Cells  Donor II Resting B  Cells  Human Th  Human Lung (clonetech)  Human Lung (clonetech)  Human Mammary (clonetech)  Human Thymus (clonetech)  (clonetech)  Jurkat (unstimulated)  AR060 Kidney  AR061 Liver  Liver (Clontech)  AR063 Lymphocytes chronic  Lymphocytes	ADOS2	D					
AR055 Heart Heart  AR056 Human Lung (clonetech)  AR057 Human Mammary (clonetech)  AR058 Human Thymus (clonetech)  AR059 Jurkat (unstimulated)  AR050 Kidney  AR061 Liver  AR063 Lymphocytes chronic  AR055 Heart  Heart  Human Lung (clonetech)  Human Mammary (clonetech)  Human Mammary (clonetech)  Human Thymus (clonetech)  AR060 Kidney  AR061 Liver  Liver (Clontech)  Liver (Clontech)  Lymphocytes	ARUSS	Donor II B-Cells /2hrs			1 1		
Cells	AR054	Donor II Pasting P Calls	Denor II Destine D		<del>                                     </del>		
AR055 Heart Heart  AR056 Human Lung (clonetech)  AR057 Human Mammary (clontech)  AR058 Human Thymus (clonetech)  (clonetech)  AR059 Jurkat (unstimulated)  AR060 Kidney  AR061 Liver  AR062 Liver (Clontech)  AR063 Lymphocytes chronic  Human Thymus (clonetech)  Human Thymus (clonetech)  All Liver  Liver (Clontech)  Liver (Clontech)  Human Thymus (clonetech)  All Liver (Clontech)  Liver (Clontech)  Liver (Clontech)	711054	Donor It Resting & Cells			1 1		
AR056 Human Lung (clonetech)  AR057 Human Mammary (clonetech)  AR058 Human Thymus (clonetech)  AR059 Jurkat (unstimulated)  AR060 Kidney  AR061 Liver  AR062 Liver (Clontech)  Human Lung (clonetech)  Human Mammary (clonetech)  Human Thymus (clonetech)  Gelonetech)  Jurkat (unstimulated)  Kidney  Kidney  AR061 Liver  Liver  AR062 Liver (Clontech)  Liver (Clontech)  AR063 Lymphocytes chronic  Lymphocytes	AR055	Heart			<del>                                     </del>		
(clonetech)  AR057 Human Mammary (clontech) (clontech)  AR058 Human Thymus Human Thymus (clonetech) (clonetech)  AR059 Jurkat (unstimulated) Jurkat (unstimulated)  AR060 Kidney Kidney  AR061 Liver Liver  AR062 Liver (Clontech) Liver (Clontech)  AR063 Lymphocytes chronic Lymphocytes							
AR057 Human Mammary (clontech) (clontech)  AR058 Human Thymus (clonetech) (clonetech)  AR059 Jurkat (unstimulated) Jurkat (unstimulated)  AR060 Kidney Kidney  AR061 Liver Liver  AR062 Liver (Clontech) Liver (Clontech)  AR063 Lymphocytes chronic Lymphocytes	10000	Transar Lang (Cionetecii)					
(clontech)         (clontech)           AR058         Human Thymus         Human Thymus           (clonetech)         (clonetech)           AR059         Jurkat (unstimulated)           Jurkat (unstimulated)         Jurkat (unstimulated)           AR060         Kidney           AR061         Liver           Liver (Clontech)         Liver (Clontech)           AR063         Lymphocytes chronic         Lymphocytes	AR057	Human Mammary	Human Mammany		+		
AR058 Human Thymus (clonetech) (clonetech)  AR059 Jurkat (unstimulated) Jurkat (unstimulated)  AR060 Kidney Kidney  AR061 Liver Liver  AR062 Liver (Clontech) Liver (Clontech)  AR063 Lymphocytes chronic Lymphocytes					1 1		1
(clonetech) (clonetech)  AR059 Jurkat (unstimulated) Jurkat (unstimulated)  AR060 Kidney Kidney  AR061 Liver Liver  AR062 Liver (Clontech) Liver (Clontech)  AR063 Lymphocytes chronic Lymphocytes	AR058				<del></del>		
AR059 Jurkat (unstimulated)  AR060 Kidney Kidney AR061 Liver Liver AR062 Liver (Clontech) AR063 Lymphocytes chronic Lymphocytes					f		
AR060 Kidney Kidney AR061 Liver Liver AR062 Liver (Clontech) Liver (Clontech) AR063 Lymphocytes chronic Lymphocytes	AR059			·· -	<del></del>		
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AR061 Liver Liver AR062 Liver (Clontech) Liver (Clontech) AR063 Lymphocytes chronic Lymphocytes	AR060	Kidney			<del></del>		
AR062 Liver (Clontech) Liver (Clontech) AR063 Lymphocytes chronic Lymphocytes					<del>                                     </del>		<del></del>
AR063 Lymphocytes chronic Lymphocytes	AR062	Liver (Clontech)			<del>                                     </del>		<del></del>
	AR063			<del></del>	1		<del></del>
		lymphocytic leukaemia				į	Į

	T	7				
10064	<del>                                     </del>	leukaemia	ļ			
AR064	Lymphocytes diffuse large					
	B cell lymphoma	diffuse large B cell				J
AR065	1. mark a see Settin 1	lymphoma	<del> </del>	<u> </u>	_	
AKUUS	Lymphocytes follicular lymphoma	Lymphocytes				
AR066	normal breast	follicular lymphoma	<del></del>	<del></del>	<del></del>	
AR067	Normal Ovarian	Normal Ovarian			<del>-</del>	
AROU/	(4004901)					
AR068	Normal Ovary 9508G045	(4004901) Normal Ovary	<del> </del>	+		<del> </del>
AROUG	1401111a1 Oval y 93080043	9508G045	1	1		
AR069	Normal Ovary 9701G208	Normal Ovary	<del> </del>	<del> </del>		<del> </del>
1	110111E OVER 37010200	9701G208	1			
AR070	Normal Ovary 9806G005	Normal Ovary	<del></del>	<del>                                     </del>	<del></del>	<del>                                      </del>
	7.5	9806G005		ļ	1	
AR071	Ovarian Cancer	Ovarian Cancer	<del>                                     </del>	<del> </del>		-
AR072	Ovarian Cancer	Ovarian Cancer	<del></del>	<del> </del>	<del></del>	<del></del>
	(9702G001)	(9702G001)		1		1
AR073	Ovarian Cancer	Ovarian Cancer				
L	(9707G029)	(9707G029)	į	1		ļ
AR074	Ovarian Cancer	Ovarian Cancer		<del> </del>		<del> </del>
	(9804G011)	(9804G011)				
AR075	Ovarian Cancer	Ovarian Cancer				
	(9806G019)	(9806G019)			1	
AR076	Ovarian Cancer	Ovarian Cancer				
15.000	(9807G017)	、(9807G017)			_	
AR077	Ovarian Cancer	Ovarian Cancer				
1 7050	(9809G001)	(9809G001)			1	
AR078	ovarian cancer 15799	ovarian cancer	Ì			
4 DOZO		15799		<u> </u>		
AR079	Ovarian Cancer	Ovarian Cancer			ļ	
AR080	17717AID Ovarian Cancer	17717AID				
ARUSU	4004664B1	Ovarian Cancer			1	1
AR081	Ovarian Cancer	4004664B1				
Autoor	4005315A1	Ovarian Cancer 4005315A1			ł	
AR082	ovarian cancer 94127303	ovarian cancer			<del> </del>	
		94127303		ŧ		
AR083	Ovarian Cancer 96069304	Ovarian Cancer		<del> </del>		
		96069304		ĺ	1	
AR084	Ovarian Cancer 9707G029	Ovarian Cancer		<del>                                     </del>	<del> </del>	
		9707G029		ļ	J i	ļ
AR085	Ovarian Cancer 9807G045	Ovarian Cancer				
		9807G045				İ
AR086	ovarian cancer 9809G001	ovarian cancer				
		9809G001				
AR087	Ovarian Cancer	Ovarian Cancer				
	9905C032RC	9905C032RC				
AR088	Ovarian cancer 9907 C00	Ovarian cancer 9907				
10000	3rd	C00 3rd				
AR089	Prostate	Prostate				
AR090	Prostate (clonetech)	Prostate (clonetech)				
AR091	prostate cancer	prostate cancer				
AR092	prostate cancer #15176	prostate cancer			1 1	
ADOD	prostate cancer #15509	#15176			ļ	
AR093	prostate cancer #15509	prostate cancer	,			f
AR094	prostate cancer #15673	#15509 prostate cancer		<del> </del>	<del>                                     </del>	
<b>ハハリンサ</b>	prostate cancer #130/3	prostate cancer #15673				
AR095	Small Intestine (Clontech)	Small Intestine			<del>                                     </del>	
	intestine (Clonicell)	(Clontech)				
	<del></del>	(Crontech)			I	

AR096	Spleen	Spleen			
AR097	Thymus T cells activated	Thymus T cells			
		activated			1
AR098	Thymus T cells resting	Thymus T cells			
<u></u>		resting			
AR099	Tonsil	Tonsil			
AR100	Tonsil geminal center	Tonsil geminal			
	centroblast	center centroblast	1		
ARIOI	Tonsil germinal center B	Tonsil germinal			
	cell	center B cell			1
AR102	Tonsil lymph node	Tonsil lymph node			
AR103	Tonsil memory B cell	Tonsil memory B			
		cell			
AR104	Whole Brain	Whole Brain			
AR105	Xenograft ES-2	Xenograft ES-2			
AR106	Xenograft-SW626	Xenograft SW626			
H0008	Whole 6 Week Old				Uni-ZAP XR
	Embryo				
H0009	Human Fetal Brain				Uni-ZAP XR
H0012	Human Fetal Kidney	Human Fetal Kidney	Kidney		Uni-ZAP XR
H0013	Human 8 Week Whole	Human 8 Week Old	Embryo		Uni-ZAP XR
	Embryo	Embryo			
H0028	Human Old Ovary	Human Old Ovary	Ovary		pBluescript
H0030	Human Placenta				Uni-ZAP XR
H0031	Human Placenta	Human Placenta	Placenta		Uni-ZAP XR
H0032	Human Prostate	Human Prostate	Prostate		Uni-ZAP XR
H0038	Human Testes	Human Testes	Testis		Uni-ZAP XR
H0040	Human Testes Tumor	Human Testes	Testis	disease	Uni-ZAP XR
		Tumor			Cin Ziu Xii
H0046	Human Endometrial	Human Endometrial	Uterus	disease	Uni-ZAP XR
	Tumor	Tumor			
H0050	Human Fetal Heart	Human Fetal Heart	Heart		Uni-ZAP XR
H0051	Human Hippocampus	Human	Brain		Uni-ZAP XR
		Hippocampus			
H0052	Human Cerebellum	Human Cerebellum	Brain		Uni-ZAP XR
H0055	Human Umbilical Vein	Human Umbilical	Umbilical		Uni-ZAP XR
		Vein Endothelial	vein		
		Cells		}	
H0056	Human Umbilical Vein,	Human Umbilical	Umbilical		Uni-ZAP XR
	Endo. remake	Vein Endothelial	vein		
		Cells	,	1	
H0057	Human Fetal Spleen				Uni-ZAP XR
H0059	Human Uterine Cancer	Human Uterine	Uterus	disease	Lambda
		Cancer		]	ZAP II
H0063	Human Thymus	Human Thymus	Thymus		Uni-ZAP XR
H0087	Human Thymus	Human Thymus			pBluescript
H0090	Human T-Cell Lymphoma	T-Cell Lymphoma	T-Cell	disease	Uni-ZAP XR
H0102	Human Whole 6 Week	Human Whole Six	Embryo		pBluescript
	Old Embryo (II), subt	Week Old Embryo			
H0111	Human Placenta,	Human Placenta	Placenta		pBluescript
	subtracted				
H0124	Human	Human	Sk Muscle	disease	Uni-ZAP XR
	Rhabdomyosarcoma	Rhabdomyosarcoma			
H0144	Nine Week Old Early	9 Wk Old Early	Embryo		Uni-ZAP XR
	Stage Human	Stage Human			
H0150	Human Epididymus	Epididymis	Testis		Uni-ZAP XR
H0156	Human Adrenal Gland	Human Adrenal	Adrenai	disease	Uni-ZAP XR
<u> </u>	Tumor	Gland Tumor	Gland		<u> </u>
H0163	Human Synovium	Human Synovium	Synovium		Uni-ZAP XR
H0165	Human Prostate Cancer,	Human Prostate	Prostate	disease	Uni-ZAP XR
	Stage B2	Cancer, stage B2			

	T					
H0166	Human Prostate Cancer, Stage B2 fraction	Human Prostate Cancer, stage B2	Prostate	T	disease	Uni-ZAP XR
H0168	Human Prostate Cancer, Stage C	Human Prostate Cancer, stage C	Prostate		disease	Uni-ZAP XR
H0169	Human Prostate Cancer,	Human Prostate	<del></del>	<del> </del>	<del></del>	
	Stage C fraction	Cancer, stage C	Prostate		disease	Uni-ZAP XR
H0170	12 Week Old Early Stage Human	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0171	12 Week Old Early Stage	Twelve Week Old	Embryo	+	<del>                                      </del>	Uni-ZAP XR
	Human, II	Early Stage Human		İ		OIII-ZAF AK
H0176	CAMA1Ee Cell Line	CAMA1Ee Cell Line	Breast	Cell Line		Uni-ZAP XR
H0178	Human Fetal Brain	Human Fetal Brain	Brain		<del>                                     </del>	Uni-ZAP XR
H0179	Human Neutrophil	Human Neutrophil	Blood	Cell Line		Uni-ZAP XR
H0181	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0182	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0188	Human Normal Breast	Human Normal Breast	Breast		<del> </del>	Uni-ZAP XR
H0194	Human Cerebellum, subtracted	Human Cerebellum	Brain		1	pBluescript
H0196	Human Cardiomyopathy, subtracted	Human Cardiomyopathy	Heart			Uni-ZAP XR
H0211	Human Prostate, differential expression	Human Prostate	Prostate			pBluescript
H0212	Human Prostate, subtracted	Human Prostate	Prostate			pBluescript
H0244	Human 8 Week Whole Embryo, subtracted	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0252	Human Osteosarcoma	Human Osteosarcoma	Bone		disease	Uni-ZAP XR
H0253	Human adult testis, large inserts	Human Adult Testis	Testis			Uni-ZAP XR
H0255	breast lymph node CDNA library	Breast Lymph Node	Lymph Node			Lambda ZAP II
H0263	human colon cancer	Human Colon Cancer	Colon		disease	Lambda ZAP II
H0266	Human Microvascular Endothelial Cells, fract. A	НМЕС	Vein	Cell Line		Lambda ZAP II
H0270	HPAS (human pancreas, subtracted)	Human Pancreas	Pancreas			Uni-ZAP XR
H0271	Human Neutrophil, Activated	Human Neutrophil - Activated	Blood	Cell Line		Uni-ZAP XR
H0294	Amniotic Cells - TNF induced	Amniotic Cells - TNF induced	Placenta	Cell Line		Uni-ZAP XR
H0295	Amniotic Cells - Primary Culture	Amniotic Cells - Primary Culture	Placenta	Cell Line	·	Uni-ZAP XR
H0310	human caudate nucleus	Brain	Brain			Uni-ZAP XR
H0316	HUMAN STOMACH	Human Stomach	Stomach			Uni-ZAP XR
H0328	human ovarian cancer	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0341	Bone Marrow Cell Line (RS4;11)	Bone Marrow Cell Line RS4;11	Bone Marrow	Cell Line		Uni-ZAP XR
H0369	H. Atrophic Endometrium	Atrophic Endometrium and myometrium				Uni-ZAP XR
H0372	Human Testes	Human Testes	Testis			pCMVSport
H0373	Human Heart	Human Adult Heart	Heart			pCMVSport

H0383	Human Prostate BPH, re-	Human Prostate				Uni-ZAP XR
H0392	H. Meningima, M1	BPH Human Meningima	h-ai-	<del></del>	<u> </u>	<del> </del>
H0399	Human Kidney Cortex, re-	Human Kidney	<u>brain</u>	<del> </del>	<del></del>	pSport1 Lambda
	rescue	Cortex				ZAP II
H0411	H Female Bladder, Adult	Human Female Adult Bladder	Bladder			pSport1
H0412	Human umbilical vein endothelial cells, IL-4 induced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0414	Ovarian Tumor I, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pSport1
H0415	H. Ovarian Tumor, II, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pCMVSport
H0427	Human Adipose	Human Adipose, left hiplipoma				pSport1
H0428	Human Ovary	Human Ovary Tumor	Ovary			pSport1
H0431	H. Kidney Medulla, re- excision	Kidney medulla	Kidney			pBluescript
H0435	Ovarian Tumor 10-3-95	Ovarian Tumor, OV350721	Ovary			pCMVSport 2.0
H0436	Resting T-Cell Library,II	T-Cells	Blood	Cell Line		pSport1
H0478	Salivary Gland, Lib 2	Human Salivary Gland	Salivary gland			pSport1
H0483	Breast Cancer cell line, MDA 36	Breast Cancer Cell line, MDA 36				pSport1
H0484	Breast Cancer Cell line, angiogenic	Breast Cancer Cell line, Angiogenic, 36T3				pSport1
H0486	Hodgkin"s Lymphoma II	Hodgkin"s Lymphoma II			disease	pCMVSport 2.0
H0494	Keratinocyte	Keratinocyte				pCMVSport 2.0
H0520	NTERA2 + retinoic acid, 14 days	NTERA2, Teratocarcinoma cell line				pSport1
H0521	Primary Dendritic Cells,	Primary Dendritic cells	-			pCMVSport 3.0
H0533	Human Stromal endometrial fibroblasts, treated w/ estradiol	Human Stromal endometrial fibroblasts, treated wit				pSport1
H0534	Human Stromal endometrial fibroblasts, treated with progesterone	Human Stromal endometrial fibroblasts, treated w/				pSport1
H0539	Pancreas Islet Cell Tumor	Pancreas Islet Cell Tumour	Pancreas		disease	pSport1
H0543	T cell helper II	Helper T cell				pCMVSport 3.0
H0544	Human endometrial stromal cells	Human endometrial stromal cells				pCMVSport 3.0
H0545	Human endometrial stromal cells-treated with progesterone	Human endometrial stromal cells-treated with proge				pCMVSport 3.0
H0546	Human endometrial stromal cells-treated with estradiol	Human endometrial stromal cells-treated with estra				pCMVSport 3.0
H0547	NTERA2 teratocarcinoma cell line+retinoic acid (14 days)	NTERA2, Teratocarcinoma cell line				pSport1

H0549	H. Epididiymus, caput &	Human		Τ	I II-: ZAD VD
11,0545	corpus	Epididiymus, caput			Uni-ZAP XR
H0550	U Caldidia	and corpus	ļ		
	H. Epididiymus, cauda	Human Epididiymus, cauda			Uni-ZAP XR
H0551	Human Thymus Stromal Cells	Human Thymus Stromal Cells			pCMVSport 3.0
H0553	Human Placenta	Human Placenta			pCMVSport
H0555	Rejected Kidney, lib 4	Human Rejected	Kidney	disease	3.0 pCMVSport
H0560	КМН2	Kidney KMH2			3.0 pCMVSport
H0587	Healing groin wound; 7.5	Groin-2/19/97	groin	disease	3.0 pCMVSport
	hours post incision			<u> </u>	3.0
H0592	Healing groin wound - zero hr post-incision (control)	HGS wound healing project; abdomen		disease	pCMVSport 3.0
H0593	Olfactory epithelium;nasalcavity	Olfactory epithelium from roof of left nasal cacit			pCMVSport 3.0
H0596	Human Colon Cancer;re- excision	Human Colon Cancer	Colon		Lambda ZAP II
H0606	Human Primary Breast Cancer;re-excision	Human Primary Breast Cancer	Breast	disease	Uni-ZAP XR
H0615	Human Ovarian Cancer Reexcision	Ovarian Cancer	Ovary	disease	Uni-ZAP XR
H0616	Human Testes, Reexcision	Human Testes	Testis		Uni-ZAP XR
H0617	Human Primary Breast Cancer Reexcision	Human Primary Breast Cancer	Breast	disease	Uni-ZAP XR
H0618	Human Adult Testes, Large Inserts, Reexcision	Human Adult Testis	Testis		Uni-ZAP XR
H0623	Human Umbilical Vein; Reexcision	Human Umbilical Vein Endothelial Cells	Umbilical vein		Uni-ZAP XR
H0632	Hepatocellular Tumor;re- excision	Hepatocellular Tumor	Liver		Lambda ZAP II
H0634	Human Testes Tumor, re- excision	Human Testes Tumor	Testis	disease	Uni-ZAP XR
H0641	LPS activated derived dendritic cells	LPS activated monocyte derived dendritic cells			pSport1
H0643	Hep G2 Cells, PCR library	Hep G2 Cells			Other
H0644	Human Placenta (re- excision)	Human Placenta	Placenta		Uni-ZAP XR
H0646	Lung, Cancer (4005313 A3): Invasive Poorly Differentiated Lung Adenocarcinoma,	Metastatic squamous cell lung carcinoma, poorly di			pSportI
H0647	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	Invasive poorly differentiated lung adenocarcinoma		disease	pSport1
H0648	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low Malignant Pot	Papillary Cstic neoplasm of low malignant potentia		disease	pSport1
H0650	B-Cells	B-Cells			pCMVSport 3.0
H0651	Ovary, Normal: (9805C040R)	Normal Ovary			pSport1
H0657	B-cells (stimulated)	B-cells (stimulated)	<del></del>		pSport1

H0658	Ovary, Cancer	9809C332- Poorty	Ovary &	T	1 42	1 - C 1
	(9809C332): Poorly differentiated	differentiate	Fallopian Tubes		disease	pSport1
	adenocarcinoma	<u> </u>				
H0659	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	Grade II Papillary Carcinoma, Ovary	Ovary		disease	pSport1
H0660	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	Poorly differentiated carcinoma, ovary			disease	pSport1
H0661	Breast, Cancer: (4004943 A5)	Breast cancer			disease	pSport1
H0662	Breast, Normal: (4005522B2)	Normal Breast - #4005522(B2)	Breast			pSport1
H0663	Breast, Cancer: (4005522 A2)	Breast Cancer - #4005522(A2)	Breast		disease	pSport1
H0664	Breast, Cancer: (9806C012R)	Breast Cancer	Breast		disease	pSport1
Н0666	Ovary, Cancer: (4004332 A2)	Ovarian Cancer, Sample #4004332A2			disease	pSportI
H0670	Ovary, Cancer(4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	Ovarian Cancer - 4004650A3				pSport1
H0672	Ovary, Cancer: (4004576 A8)	Ovarian Cancer(4004576A8)	Ovary			pSport1
H0673	Human Prostate Cancer, Stage B2; re-excision	Human Prostate Cancer, stage B2	Prostate			Uni-ZAP XR
H0674	Human Prostate Cancer, Stage C; re-excission	Human Prostate Cancer, stage C	Prostate			Uni-ZAP XR
H0676	Colon, Cancer: (9808C064R)-total RNA	Colon Cancer 9808C064R				pCMVSport 3.0
H0678	screened clones from placental library	Placenta	Placenta			Other
H0683	Ovarian Serous Papillary Adenocarcinoma	Serous papillary adenocarcinoma, stage 3C (9804G0)				pCMVSport 3.0
H0685	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-3	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-				pCMVSport 3.0
H0686	Adenocarcinoma of Ovary, Human Cell Line	Adenocarcinoma of Ovary, Human Cell Line, # SW-626				pCMVSport 3.0
H0687	Human normal ovary(#9610G215)	Human normal ovary(#9610G215)	Ovary			pCMVSport 3.0
H0688	Human Ovarian Cancer(#9807G017)	Human Ovarian cancer(#9807G017), mRNA from Maura Ru				pCMVSport 3.0
H0689	Ovarian Cancer	Ovarian Cancer, #9806G019				pCMVSport 3.0
H0690	Ovarian Cancer, # 9702G001	Ovarian Cancer, #9702G001				pCMVSport 3.0
S0004	Prostate	Prostate BPH	Prostate			Lambda ZAP II
S0013	Prostate	Prostate	prostate			Uni-ZAP XR
S0014	Kidney Cortex	Kidney cortex	Kidney			Uni-ZAP XR
S0026	Stromal cell TF274	stromal cell	Bone marrow	Cell Line		Uni-ZAP XR
S0028	Smooth muscle,control	Smooth muscle	Pulmanary artery	Cell Line		Uni-ZAP XR
S0042	Testes	Human Testes		LI		ZAP Express

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S0044	Prostate BPH	prostate BPH	Prostate		disease	Uni-ZAP XR
S0052	neutrophils control	human neutrophils	blood	Cell Line		Uni-ZAP XR
S0112	Hypothalamus		Brain			Uni-ZAP XR
S0134	Apoptotic T-cell	apoptotic cells		Cell Line		Uni-ZAP XR
S0146	prostate-edited	prostate BPH	Prostate			Uni-ZAP XR
S0148	Normal Prostate	Prostate	prostate	_		Uni-ZAP XR
S0150	LNCAP prostate cell line	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
S0152	PC3 Prostate cell line	PC3 prostate cell		-		Uni-ZAP XR
S0168	Prostate/LNCAP, subtraction I	PC3 prostate cell			<del></del>	pBluescript
S0174	Prostate-BPH subtracted II	Human Prostate BPH				pBluescript
S0176	Prostate, normal, subtraction I	Prostate	prostate			Uni-ZAP XR
S0188	Prostate,BPH, Lib 2	Human Prostate BPH			disease	pSport1
S0190	Prostate BPH,Lib 2, subtracted	Human Prostate				pSport1
S0212	Bone Marrow Stromal	ВРН		ļ		
30212	Cell, untreated	Bone Marrow Stromal Cell,untreated				pSport1
S0222	H. Frontal	H. Brain, Frontal	Brain		disease	LI-: ZADVD
	cortex,epileptic;re- excision	Cortex, Epileptic	Diam		disease	Uni-ZAP XR
S0242	Synovial Fibroblasts (Il1/TNF), subt	Synovial Fibroblasts			···	pSport1
S0274	PCMIX	PCMIX (Human Cerebellum)	Brain			PCRII
S0282	Brain Frontal Cortex, re- excision	Brain frontal cortex	Brain			Lambda ZAP II
S0284	7TMCTT (Testis)	7TMCTP (Placenta)	Testis			PCRII
S0286	7TMCTP (Placenta)	H7MCTP (PLACENTA)	Placenta		· , , <u> </u>	PCRII
S0294	Larynx tumor	Larynx tumor	Larynx,vocal cord		disease	pSport1
S0326	Mammary Gland	Mammary Gland	Whole mammary gland			pSport1
S0328	Palate carcinoma	Palate carcinoma	Uvula		disease	pSport1
S0352	Larynx Carcinoma	Larynx carcinoma			disease	pSport1
S0354	Colon Normal II	Colon Normal	Colon		uisease	
S0358	Colon Normal III	Colon Normal	Colon			pSport1
S0360	Colon Tumor II	Colon Turnor	Colon		disease	pSport1
S0374	Normal colon	Normal colon	Colon		disease	pSport1
S0380	Pancreas Tumor PCA4 Tu	Pancreas Tumor PCA4 Tu			disease	pSport1 pSport1
S0396	Uterus; normal	Uterus; normal			<del> </del>	nSnort1
S0398	Testis; normal	Testis; normal				pSport1
S0412	Temporal cortex- Alzheizmer; subtracted	Temporal cortex,			disease	pSport1 Other
S0422	Mo7e Cell Line GM-CSF treated (1ng/ml)	Mo7e Cell Line GM-CSF treated (lng/ml)				pCMVSport 3.0
S0424	TF-1 Cell Line GM-CSF Treated	TF-1 Cell Line GM-CSF Treated				pSport1
S0442	Colon Normal	Colon Normal				pSport1
S0444	Colon Tumor	Colon Turnour	<del></del>	<del>-</del>	disease	pSport1
S0454	Placenta	Placenta	Placenta	<del>+</del>	a locase	pSport1
S0456	Tongue Normal	Tongue Normal	, , , , , , , , , , , , , , , , , , , ,	<del></del>		pSport1
S0460	Thyroid Tumour	Thyroid Tumour	··· <del>-  </del>	<del></del>		pSport1 pSport1
		-11/1-010 1 11/11/041				Pahotri

T0010	Human Infant Brain	Human Infant Brain	<del></del>	T T	Other
T0041	Jurkat T-cell G1 phase	Jurkat T-cell			pBluescript
, T006B	N. 16				SK-
T0068	Normal Ovary, Premenopausal	Normal Ovary, Premenopausal			pBluescript
T0069	Human Uterus, normal	Human Uterus,		<del>  </del>	SK- pBluescript
	<u>i</u>	normal	1		SK-
L0005	Clontech human aorta				1
1,0001	polyA+ mRNA (#6572)				
L0021	Human adult (K.Okubo) human adult testis		<del></del>	<u> </u>	
L0040	Human colon mucosa				<u> </u>
L0040	Human epidermal		<del></del>		
200	keratinocyte				
L0060	Human thymus NSTH II			<del>                                     </del>	<del></del>
L0070	Selected chromosome 21		†		
	cDNA library				
L0109	Human brain cDNA	brain			
L0142	Human placenta cDNA (TFujiwara)	placenta			
L0143	Human placenta polyA+ (TFujiwara)	placenta			
L0151	Human testis (C. De Smet)	testis			
L0157	Human fetal brain (TFujiwara)		brain		+
L0163	Human heart cDNA		heart		
L0351	(YNakamura) Infant brain, Bento Soares				
					BA, M13- derived
L0352	Normalized infant brain, Bento Soares				BA, M13- derived
L0361	Stratagene ovary (#937217)		ovary		Bluescript SK
L0362	Stratagene ovarian cancer (#937219)				Bluescript SK-
L0363	NCI_CGAP_GC2	germ cell tumor			Bluescript SK-
L0365	NCI_CGAP_Phe1	pheochromocytoma			Bluescript SK-
L0366	Stratagene schizo brain S11	schizophrenic brain S-I1 frontal lobe			Bluescript SK-
L0367	NCI_CGAP_Sch1	Schwannoma tumor			Bluescript
					SK-
L0369	NCI_CGAP_AA1	adrenal adenoma	adrenal gland		Bluescript SK-
L0371	NCI_CGAP_Br3	breast turnor	breast	,	Bluescript SK-
L0372	NCI_CGAP_Co12	colon tumor	colon		Bluescript SK-
L0373	NCI_CGAP_Col1	· tumor	colon		Bluescript
L0374	NCI_CGAP_Co2	tumor	colon		SK- Bluescript
L0375	NCI_CGAP_Kid6	kidney tumor	kidney		SK- Bluescript
L0376	NCI_CGAP_Larl	larynx	larynx		SK- Bluescript
L0378	NCI_CGAP_Lu1	lung tumor	lung		SK- Bluescript
L0380	NCI_CGAP_HN1	conome : a - 11	limah = -d-		SK-
הפנחד	NCI_COAP_HNI	squamous cell	lymph node		Bluescript

		carcinoma	T	т	<del></del>	1 614
L0381	NCI_CGAP_HN4	squamous cell	pharynx	<del> </del>	<del> </del> -	SK-
	1.0.2007.1.2.1114	carcinoma	Pilalylix			Bluescript
L0383	NCI CGAP Pr24	invasive tumor (cell	prostate	<del> </del>	<del>-</del>	SK- Bluescript
		line)	prostate	ĺ	]	SK-
L0411	1-NIB				<del> </del>	Lafmid BA
L0435	Infant brain, LLNL array					lafmid BA
	of Dr. M. Soares INIB			1	1	i i i i i i i i i i i i i i i i i i i
L0438	normalized infant brain	total brain	brain		j	lafmid BA
	cDNA			<u></u>		
L0439	Soares infant brain 1NIB		whole brain			Lafmid BA
L0441	2HB3MK					Lafmid BK
L0455	Human retina cDNA	retina	eye			lambda gt10
1	randomly primed sublibrary			ļ		
L0462	WATM1		<u> </u>			
L0465	TEST1, Human adult	<del> </del>			<del></del>	lambda gt11
20403	Testis tissue		1			lambda
L0470	BL29 Burkitt"s	<del> </del>		-		nm1149
	lymphoma, Pascalis			·		lambda ZAP 2
L	Sideras					2
L0471	Human fetal heart,					Lambda
	Lambda ZAP Express					ZAP Express
L0475	KG1-a Lambda Zap			KG1-a		Lambda Zap
	Express cDNA library					Express
T 0400	G					(Stratagene)
L0480	Stratagene cat#937212 (1992)					Lambda
	(1992)					ZAP,
	1					pBluescript
L0483	Human pancreatic islet					SK(-) Lambda
	}			- 1		ZAPII
L0485	STRATAGENE Human	skeletal muscle	leg muscle			Lambda
	skeletal muscle cDNA					ZAPII
	library, cat. #936215.					
L0492	Human Genomic					pAMP
L0509	NCI_CGAP_Lu26	invasive	lung			pAMP1
L0512	NCL CCAR O.26	adenocarcinoma				
LU312	NCI_CGAP_Ov36	borderline ovarian	ovary	1		pAMP1
L0513	NCI_CGAP_Ov37	carcinoma early stage papillary				
20313	Nei_cdAi_cv3/	serous carcinoma	ovary			pAMPI
L0515	NCI_CGAP_Ov32	papillary serous	ovary			pAMP1
		carcinoma	Ovary			PAMEI
L0516	Chromosome 19p12-p13.1					pAMP10
	exon			ł	J	
L0517	NCI_CGAP_Pr1					pAMP10
L0518	NCI_CGAP_Pr2					pAMP10
L0519	NCI_CGAP_Pr3					pAMP10
L0520	NCI_CGAP_AIVI	alveolar	1	T		pAMP10
1.0521	NCL CCAR F1	rhabdomyosarcoma				
L0521 L0522	NCI_CGAP_Ew1 NCI_CGAP_Kid1	Ewing"s sarcoma				pAMP10
L0522	NCI_CGAP_Lip2	kidney liposarcoma				pAMP10
L0523	NCI CGAP Lil	liver				pAMP10
L0524	NCI_CGAP_Pr12	metastatic prostate				pAMP10
		bone lesion	1			pAMP10
L0527	NCI CGAP_Ov2	ovary		<del></del>		pAMP10
L0528	NCI CGAP Pr5	prostate				pAMP10
L0529	NCI CGAP Pr6	prostate		<del></del>	-	pAMP10
L0532	NCI_CGAP_Thy1	thyroid				pAMP10

L0533	NCI_CGAP_HSCI	stem cells	bone marrow	71	<del></del>	pAMP10
L0534	Chromosome 7 Fetal Brain cDNA Library	brain	brain			pAMP10
L0536	NCI_CGAP_Br4	normal ductal tissue	breast	<u> </u>		pAMP10
L0539	Chromosome 7 Placental cDNA Library		placenta			pAMP10
L0542	NCI_CGAP_Pri1	normal prostatic epithelial cells	prostate			pAMP10
L0547	NCI CGAP Pr16	tumor	prostate			pAMP10
L0558	NCI_CGAP_Ov40	endometrioid ovarian metastasis	ovary		A .	pAMP10
L0565	Normal Human Trabecular Bone Cells	Bone	Hip			pBluescript
L0581	Stratagene liver (#937224)		liver			pBluescript SK
L0586	HTCDLI					pBluescript SK(-)
L0587	Stratagene colon HT29 (#937221)					pBluescript SK-
L0588	Stratagene endothelial cell 937223					pBluescript SK-
L0589	Stratagene fetal retina 937202			<del> </del>		pBluescript SK-
L0590	Stratagene fibroblast (#937212)	·				pBluescript SK-
L0591	Stratagene HeLa cell s3 937216					pBluescript
L0592	Stratagene hNT neuron (#937233)					pBluescript SK-
L0593	Stratagene neuroepithelium (#937231)					pBluescript SK-
L0594	Stratagene neuroepithelium NT2RAMI 937234					pBluescript SK-
L0595	Stratagene NT2 neuronal precursor 937230	neuroepithelial cells	brain			pBluescript SK-
L0596	Stratagene colon (#937204)		colon			pBluescript SK-
L0597	Stratagene corneal stroma (#937222)		cornea		<del> </del>	pBluescript SK-
L0598	Morton Fetal Cochlea	cochlea	ear			pBluescript SK-
L0599	Stratagene lung (#937210)		lung			pBluescript SK-
L0600	Weizmann Olfactory Epithelium	olfactory epithelium	nose			pBluescript SK-
L0601	Stratagene pancreas (#937208)		pancreas			pBluescript SK-
L0602	Pancreatic Islet	pancreatic islet	pancreas			pBluescript SK-
L0603	Stratagene placenta (#937225)		placenta			pBluescript SK-
L0604	Stratagene muscle 937209	muscle	skeletal muscle			pBluescript SK-
L0605	Stratagene fetal spleen (#937205)	fetal spleen	spleen	<del></del>		pBluescript SK-
L0606	NCI_CGAP_Lym5	follicular lymphoma	lymph node		<del> </del>	pBluescript SK-
L0608	Stratagene lung carcinoma 937218	lung carcinoma	lung	NCI-H69		pBluescript SK-

L0612	Schiller	oligodendroglioma	brain	<del></del>	
500.5	oligodendroglioma	ongodendrognoma	brain		pBluescript SK-
					(Stratagene)
L0617	Chromosome 22 exon	<del></del>		<del> </del>	pBluescriptII
					KS+
L0618	Chromosome 9 exon				pBluescriptll
			Ĺ	[	KS+
L0623	HM3	pectoral muscle			pcDNAII
		(after mastectomy)			(Invitrogen)
L0626	NCI_CGAP_GC1	bulk germ cell			pCMV-
L0635	NGL GG ( P. P.)	seminoma		· .	SPORT2
L0033	NCI_CGAP_PNS1	dorsal root ganglion	peripheral		pCMV-
1			nervous	1	SPORT4
L0637	NCI_CGAP_Bm53	three pooled	system		
20057	Noi_com _bills	meningiomas	brain		pCMV-
L0638	NCI_CGAP_Bm35	tumor, 5 pooled (see	brain	<del> </del>	SPORT6
		description)	Diani		pCMV- SPORT6
L0639	NCI_CGAP_Brn52	tumor, 5 pooled (see	brain	<del> </del>	pCMV-
L		description)		[	SPORT6
L0642	NCI_CGAP_Co18	moderately	colon		pCMV-
		differentiated	İ		SPORT6
7011		adenocarcinoma			
L0646	NCI_CGAP_Co14	moderately-	colon		pCMV-
		differentiated			SPORT6
L0647	NCI_CGAP_Sar4	adenocarcinoma	ļ		
1 20047	INCI_COAT_Sal4	five pooled sarcomas, including	connective tissue		pCMV-
		myxoid liposarcoma	ussue		SPORT6
L0649	NCI_CGAP_GU1	2 pooled high-grade	genitourinary		pCMV-
Ì		transitional cell	tract		SPORT6
		tumors			SI OKIO
L0655	NCI_CGAP_Lym12	lymphoma,	lymph node		pCMV-
		follicular mixed			SPORT6
10666	1101 001 7 0 00	small and large cell			
L0656	NCI_CGAP_Ov38	normal epithelium	ovary		pCMV-
L0657	NCI_CGAP_Ov23	tumon 5 montal (and			SPORT6
2003,	Nei_edal_evzs	tumor, 5 pooled (see description)	ovary	l	pCMV-
L0658	NCI_CGAP_Ov35	tumor, 5 pooled (see	ovary		SPORT6 pCMV-
		description)	Ovary		SPORT6
L0659	NCI_CGAP Pan1	adenocarcinoma	pancreas		pCMV-
					SPORT6
L0661	NCI_CGAP_Mel15	malignant	skin		pCMV-
		melanoma,			SPORT6
		metastatic to lymph			
L0662	NCI_CGAP_Gas4	node poorly differentiated			
L0002	NCI_COAF_Gas4	adenocarcinoma	stomach		pCMV-
		with signet r		l l	SPORT6
L0663	NCI_CGAP_Ut2	moderately-	uterus	<del></del>	pCMV-
		differentiated			SPORT6
		endometrial			
		adenocarcino			
L0664	NCI_CGAP_Ut3	poorly-differentiated	uterus		pCMV-
		endometrial			SPORT6
L0665	NCI_CGAP_Ut4	adenocarcinoma,			
F0002	MOI_COMF_UI4	serous papillary carcinoma, high	uterus		pCMV-
		grade, 2 pooled t	ļ	ļ	SPORT6
L0666	NCI_CGAP_Ut1 .	well-differentiated	uterus		pCMV-
	<u> </u>	endometrial		1	SPORT6
t					10,0,0,0

		adenocarcinoma, 7		<del></del>	<del></del>
L0667	NCI_CGAP_CMLI	myeloid cells, 18	whole blood	<del> </del>	- C) (1)/
20007	MCI_COAF_CWE	pooled CML cases,	Whole blood		pCMV-
-		BCR/ABL rearra			SPORT6
L0686	Stanlay Francis CN 12		<del>                                     </del>		
L0000	Stanley Frontal SN pool 2	frontal lobe (see	brain		pCR2.1-
ļ	,	description)	}	1	TOPO
1000				<u> </u>	(Invitrogen)
L0697	Testis 1				PGEM
			L	<u>l</u> I	5zf(+)
L0698	Testis 2				PGEM
					5zf(+)
L0700	Outward Alu-primed				pGEM-3Z
L	hncDNA library		Į		1,
L0717	Gessler Wilms tumor				pSPORT1
L0731	Soares_pregnant_uterus_	<del></del>	uterus	† <del>-</del> -	pT7T3-Pac
	NbHPU				p1/13-1 ac
L0738	Human colorectal cancer			<del> </del>	pT7T3D
L0740	Soares melanocyte	melanocyte		<del> </del>	pT7T3D
	2NbHM	meianooyte		1	(Pharmacia)
İ			•	l i	with a
ŀ	İ			i i	modified
1				1	
L0741	Soares adult brain		brain	<del> </del>	polylinker
207-71	N2b4HB55Y		Diam	1	pT7T3D
	1120-1115551				(Pharmacia)
1	į l			]	with a
				1 1	modified
L0742	Soares adult brain		,		polylinker
L0742	N2b5HB55Y		brain	ļ .	pT7T3D
1	NZOSHBSSY				(Pharmacia)
ŀ					with a
				l i	modified
L0743	C				polylinker
L0743	Soares breast 2NbHBst		breast		pT7T3D
ł					(Pharmacia)
					with a
1		İ			modified
					polylinker
L0744	Soares breast 3NbHBst		breast		pT7T3D
					(Pharmacia)
					with a
					modified
					polylinker
L0745	Soares retina N2b4HR	retina	eye		pT7T3D
					(Pharmacia)
	- 1				with a
			l		modified
					polylinker
L0746	Soares retina N2b5HR	retina	eye		pT7T3D
					(Pharmacia)
1				j	with a
				1	modified
<u> </u>					polylinker
L0747	Soares_fetal_heart_NbHH		heart		pT7T3D
	19W			1	(Pharmacia)
	l l			1	with a
					modified
لــــــا		· · · · · · · · · · · · · · · · · · ·			polylinker
L0748	Soares fetal liver spleen		Liver and		pT7T3D
	INFLS		Spleen		(Pharmacia)
	İ	Į			with a
	}	[		1	modified
					polylinker

L0749	Soares_fetal_liver_spleen	T	T	<del></del>	
20749	INELS STEER TIVET SPICE		Liver and		pT7T3D
	_INFLS_S1	i	Spleen	1	(Pharmacia)
1		l		1 1	with a
1	1				modified
L					polylinker
L0750	Soares_fetal_lung_NbHL1		lung		pT7T3D
ł	19w	[	1	1 1	(Pharmacia)
			1		with a
1				1	1
				1 1	modified
L0751	Soares ovary tumor	ovarian tumor	<del> </del>	<del> </del>	polylinker
1 20,31	NbHOT	ovarian tumor	ovary		pT7T3D
1	NUNO		1	]	(Pharmacia)
1		1	İ	1	with a
ı	•				modified
1.0000					polylinker
L0752	Soares_parathyroid_tumor	parathyroid tumor	parathyroid	1	pT7T3D
	_NbHPA		gland		(Pharmacia)
İ		Į.			with a
ŀ				] ]	modified
					polylinker
L0753	Soares_pineal_gland_N3H		pineal gland		pT7T3D
	PG	1		]	(Pharmacia)
1	]				with a
1	İ		1	i i	modified
L0754	Soares placenta Nb2HP		placenta	<del> </del>	polylinker
20,31	Source placelita (40211)		ріасепіа		pT7T3D
					(Pharmacia)
Ī				l i	with a
					modified
10755			ļ		polylinker
L0755	Soares_placenta_8to9wee	,	placenta	<b> </b>	pT7T3D
İ	ks_2NbHP8to9W			]	(Pharmacia)
1					with a
					modified
	· .				polylinker
L0756	Soares_multiple_sclerosis	multiple sclerosis			pT7T3D
	_2NbHMSP	lesions			(Pharmacia)
	-		1		with a
					modified
					polylinker
					V TYPE
L0757	Soares_senescent_fibrobla	senescent fibroblast			
	sts_NbHSF	Schoolent Horograft			pT7T3D
İ	365_1101101			<b>]</b>	(Pharmacia)
1				ľ	with a
					modified
					polylinker
L0758	Conne Antin NIVE				V_TYPE
LU/38	Soares_testis_NHT				pT7T3D-Pac
	ļ <b>1</b>		İ		(Pharmacia)
			i		with a
	· •	ľ	l	1	modified
					polylinker
L0759	Soares_total_fetus_Nb2H				pT7T3D-Pac
	F8_9w		ľ	[	(Pharmacia)
			l		with a
			1	1	modified
	l		į	1	polylinker
L0761	NCI_CGAP_CLL1	B-cell, chronic		<del></del>	pT7T3D-Pac
		lymphotic leukemia	ļ		(Pharmacia)
		.,priotic icakciilla			with a
				1	
					modified
L0762	NCI_CGAP_Brl.1	breast		<del></del>	polylinker
20,02	1101 COUT DITI	Ureast			pT7T3D-Pac

	T		1		(D)
			1		(Pharmacia) with a
					modified
			}		polylinker
L0763	NCI_CGAP_Br2	breast			pT7T3D-Pac
1					(Pharmacia)
					with a
ŀ			ĺ		modified
L0764	NCI_CGAP_Co3	colon			polylinker
20704	NC:_CGAL_CGS	Colon		1	pT7T3D-Pac (Pharmacia)
			ŀ		with a
İ			ļ		modified
					polylinker
L0765	NCI_CGAP_Co4	colon			pT7T3D-Pac
				1 1	(Pharmacia)
	1	1		1	with a
					modified
L0766	NCI_CGAP_GCB1	germinal center B			polylinker
L0700	NCI_COAF_GCBI	cell			pT7T3D-Pac
		Cen			(Pharmacia) with a
					modified
					polylinker
L0767	NCI_CGAP_GC3	pooled germ cell			pT7T3D-Pac
ĺ	ł	turnors		1	(Pharmacia)
ŀ					with a
					modified
L0768	NCI_CGAP_GC4			-	polylinker
L0708	NCI_COAP_GC4	pooled germ cell tumors			pT7T3D-Pac
		tuniors			(Pharmacia) with a
				1	modified
				1	polylinker
L0769	NCI_CGAP_Bm25	anaplastic	brain		pT7T3D-Pac
		oligodendroglioma			(Pharmacia)
					with a
					modified
L0770	NCI_CGAP_Bm23	glioblastoma	brain	1	polylinker
1 20770	NCI_COAT_BIII23	(pooled)	Drain	1	pT7T3D-Pac (Pharmacia)
		(pooled)		1	with a
					modified
					polylinker
L0771	NCI_CGAP_Co8	adenocarcinoma	colon		pT7T3D-Pac
				1	(Pharmacia)
					with a
					modified
L0772	NCI_CGAP_Co10	colon tumor RER+	colon	<del> </del>	polylinker pT7T3D-Pac
202	//ci_cc/ii _cc/i	COION TAINOI REIC	COIOII	]	(Pharmacia)
j .				}	with a
[				1	modified
				<u> </u>	polylinker
L0773	NCI_CGAP_Co9	colon tumor RER+	colon		pT7T3D-Pac
		1		1	(Pharmacia)
					with a
]		]			modified
L0774	NCI_CGAP_Kid3	<del>                                     </del>	kidney	<del> </del>	polylinker pT7T3D-Pac
50777	1101_00A1_KI03		Kidiley		(Pharmacia)
					with a
				]	modified
	L	1		<u> </u>	modified

		<u> </u>		Г	polylinker
L0775	NCI_CGAP_Kid5	2 pooled tumors	kidney		pT7T3D-Pac
		(clear cell type)			(Pharmacia)
			1	1	with a
			ľ	1	modified
					polylinker
L0776	NCI CGAP Lu5	carcinoid	lung		pT7T3D-Pac
					(Pharmacia)
		ļ	l .	1	with a
					modified
		į	<b>\</b>	(	polylinker
L0777	Soares_NhHMPu_S1	Pooled human	mixed (see		pT7T3D-Pac
DOTT	Joanes_Iviii ivii a_o:	melanocyte, fetal	below)		(Pharmacia)
		heart, and pregnant	1		with a
		nount, and program	<u> </u>		modified
				1	polylinker
L0779	Soares_NFL_T_GBC_S1		pooled	ļ	pT7T3D-Pac
LUIII	30arcs_141 L_1_0DC_31		poored		(Pharmacia)
					with a
		1	ì	1	modified
					polylinker
1.0700	Carra NCE ER OW OT			<del> </del>	
L0780	Soares_NSF_F8_9W_OT	İ	pooled		pT7T3D-Pac
	_PA_P_S1	}	1	] [	(Pharmacia) with a
					modified
		ĺ	İ		
1.0700	NO. COLD DOL	<del> </del>			polylinker
L0782	NCI_CGAP_Pr21	normal prostate	prostate		pT7T3D-Pac
			1		(Pharmacia)
					with a
					modified
					polylinker
L0783	NCI_CGAP_Pr22	normal prostate	prostate		pT7T3D-Pac
		ł	ļ		(Pharmacia)
					with a
			l		modified
			<u></u>	<u> </u>	polylinker
L0786	Soares_NbHFB		whole brain		pT7T3D-Pac
		l	l	[ [	(Pharmacia)
	·	•			with a
į		ļ	ļ		modified
	NO. 0012 B 11	ļ	<del> </del>		polylinker
L0787	NCI_CGAP_Sub1				pT7T3D-Pac
			1	[	(Pharmacia)
		1			with a
			Į.	[ ]	modified
1.0533	NO. 0010 5 15		<del> </del>	<del> </del>	polylinker
L0788	NCI_CGAP_Sub2		1		pT7T3D-Pac
		Í		]	(Pharmacia)
			ì	1	with a
			1		modified
		ļ		<del>  </del>	polylinker
L0789	NCI_CGAP_Sub3		I		pT7T3D-Pac
			1		(Pharmacia)
		ł	1	<b> </b>	with a
					modified
			ļ		polylinker
L0790	NCI_CGAP_Sub4	1			pT7T3D-Pac
		{			(Pharmacia)
	{	1			with a
		1			modified
			<u> </u>		polylinker
	1101 0010 016	1	1	1 -	pT7T3D-Pac
L0791	NCI_CGAP_Sub5	1	1	i l	(Pharmacia)

	with a
	modified
L0792 NCI_CGAP_Sub6	polylinker
LU792 NCI_CGAP_SUDO	pT7T3D-Pac
	(Pharmacia)
	with a
	modified
	polylinker
L0794 NCI_CGAP_GC6 pooled germ cell	pT7T3D-Pac
tumors	(Pharmacia)
	with a
	modified
	polylinker
L0796 NCI_CGAP_Bm50 medulloblastoma brain	pT7T3D-Pac
	(Pharmacia)
	with a
	modified
	polylinker
L0800 NCI_CGAP_Co16 colon turnor, RER+ colon	pT7T3D-Pac
	(Pharmacia)
	with a
	modified
	polylinker
L0803 NCI_CGAP_Kid11 kidney	pT7T3D-Pac
	(Pharmacia)
	with a
	modified
	polylinker
L0804 NCI_CGAP_Kid12 2 pooled tumors kidney	pT7T3D-Pac
(clear cell type)	(Pharmacia)
	with a
	modified
	polylinker
L0805 NCI_CGAP_Lu24 carcinoid lung	pT7T3D-Pac
	(Pharmacia)
	with a
	modified
	polylinker
L0806 NCI_CGAP_Lu19 squamous cell lung	pT7T3D-Pac
carcinoma, poorly	(Pharmacia)
differentiated (4	with a
	modified
	polylinker
L0807 NCI_CGAP_Ov18 fibrotheoma ovary	pT7T3D-Pac
	(Pharmacia)
	with a
	modified
	polylinker
L0809 NCI_CGAP_Pr28 prostate	pT7T3D-Pac
	(Pharmacia)
	with a
	modified
	polylinker

## TABLE 5

OMINA	
OMIM	Description
Reference	O to the bird
102200	Somatotrophinoma
102480	Male infertility due to acrosin deficiency
102770	Myoadenylate deaminase deficiency
103050	Autism, succinylpurinemic
103050	Adenylosuccinase deficiency
104770	Amyloidosis, secondary, susceptibility to
106100	Angioedema, hereditary
106150	Hypertension, essential, susceptibility to
106150	Preeclampsia, susceptibility to
106300	Ankylosing spondylitis
107670	Apolipoprotein A-II deficiency
107741	Hyperlipoproteinemia, type III
107910	Virilization, maternal and fetal, from placental aromatase
	deficiency
107910	Gynecomastia, familial, due to increased aromatase activity
108725	Atherosclerosis, susceptibility to
108800	Atrial septal defect, secundum type
108962	Hypertension, salt-resistant
109270	Renal tubular acidosis, distal, 179800
109270	Spherocytosis, hereditary
109270	[Acanthocytosis, one form]
109270	[Elliptocytosis, Malaysian-Melanesian type]
109270	Hemolytic anemia due to band 3 defect
109400	Basal cell nevus syndrome
109700	Hemodialysis-related amyloidosis
110700	Vivax malaria, susceptibility to
113100	Brachydactyly, type C
113705	Ovarian cancer
113705	Breast cancer-1
113721	Breast cancer
113900	Heart block, progressive familial, type I
114240	Muscular dystrophy, limb-girdle, type 2A, 253600
116806	Colorectal cancer
118485	Polycystic ovary syndrome with hyperandrogenemia
118504	Epilepsy, benign neonatal, type 1, 121200
118504	Epilepsy, nocturnal frontal lobe, 600513
118800	Choreoathetosis, familial paroxysmal
120110	Metaphyseal chondrodysplasia, Schmid type
120120	Epidermolysis bullosa dystrophica, dominant, 131750
120120	Epidermolysis bullosa dystrophica, technilant, 131750
120120	Epidermolysis bullosa dystropinea, recessive, 220000  Epidermolysis bullosa, pretibial, 131850
120120	Ehlers-Danlos syndrome, type I, 130000
120213	Enners-Damos syndrome, type I, 150000

120215	
120215	Ehlers-Danlos syndrome, type II, 130010
120280	Stickler syndrome, type III
120280	Marshall syndrome, 154780
120290	OSMED syndrome, 215150
120290	Stickler syndrome, type II, 184840
120435	Muir-Torre syndrome, 158320
120435	Colorectal cancer, hereditary, nonpolyposis, type 1 Ovarian cancer
120436	Muir-Torre family cancer syndrome, 158320
120436	Turcot syndrome with glioblastoma, 276300
120436	Colorectal cancer, hereditary nonpolyposis, type 2
120700	C3 deficiency
120810	C4 deficiency
120820	C4 deficiency
120940	C9 deficiency
121011	Deafness, autosomal dominant 3, 601544
121011	Deafness, autosomal recessive 1, 220290
121014	Heterotaxia, visceroatrial, autosomal recessive
122720	Nicotine addiction, protection from
122720	Coumarin resistance, 122700
123620	Cataract, cerulean, type 2, 601547
123660	Cataract, Coppock-like
124030	Parkinsonism, susceptibility to
124030	Debrisoquine sensitivity
124200	Darier disease (keratosis follicularis)
125270	Porphyria, acute hepatic
125270	Lead poisoning, susceptibility to
125660	Myopathy, desminopathic
125660	Cardiomyopathy
125852	Insulin-dependent diabetes mellitus-2
126340	Xeroderma pigmentosum, group D, 278730
126391	DNA ligase I deficiency
126452	Autonomic nervous system dysfunction
126452	[Novelty seeking personality]
126600	Drusen, radial, autosomal dominant
126650	Chloride diarrhea, congenital, Finnish type, 214700
126650	Colon cancer
128100	Dystonia-1, torsion
129500	Ectodermal dysplasia, hidrotic
130410	Glutaricaciduria, type IIB
131100	Multiple endocrine neoplasia I
131100	Prolactinoma, hyperparathyroidism, carcinoid syndrome
131100	Carcinoid tumor of lung
131242	Shah-Waardenburg syndrome, 277580
132800	Basal cell carcinoma
132800	Epithelioma, self-healing, squamous 1, Ferguson-Smith type

133171	[Erythrocytosis, familial], 133100
133450	Neuroepithelioma
133450	Ewing sarcoma
133701	Exostoses, multiple, type 2
133780	Vitreoretinopathy, exudative, familial
134580	Factor XIIIB deficiency
134790	Hyperferritinemia-cataract syndrome, 600886
134797	Shprintzen-Goldberg syndrome, 182212
134797	Ectopia lentis, isolated
134797	Marfan syndrome, 154700
135300	Fibromatosis, gingival
135940	Ichthyosis vulgaris, 146700
136350	Pfeiffer syndrome, 101600
136435	
150455	Ovarian dysgenesis, hypergonadotropic, with normal karyotype, 233300
136550	Macular dystrophy, North Carolina type
136836	Fucosyltransferase-6 deficiency
137350	Amyloidosis, Finnish type, 105120
138079	Hyperinsulinism, familial, 602485
138079	MODY, type 2, 125851
138320	Hemolytic anemia due to glutathione peroxidase deficiency
138570	Non-insulin dependent diabetes mellitus, susceptibility to
138720	Bernard-Soulier syndrome, type B
138981	Pulmonary alveolar proteinosis, 265120
139191	Growth hormone deficient dwarfism
139320	Pituitary ACTH secreting adenoma
139320	Pseudohypoparathyroidism, type Ia, 103580
139320	Somatotrophinoma
139320	McCune-Albright polyostotic fibrous dysplasia, 174800
141750	Alpha-thalassemia/mental retardation syndrome, type 1
141800	Methemoglobinemias, alpha-
141800	Thalassemias, alpha-
141800	Erythremias, alpha-
141800	Heinz body anemias, alpha-
141850	Thalassemia, alpha-
141850	Erythrocytosis
141850	Heinz body anemia
141850	Hemoglobin H disease
141850	Hypochromic microcytic anemia
141900	Methemoglobinemias, beta-
141900	Sickle cell anemia
141900	Thalassemias, beta-
141900	
	Erythremias, beta-
141900	HPFH, deletion type

142000	Thalassemia due to Hb Lepore
142000	Thalassemia, delta-
142200	HPFH, nondeletion type A
142250	HPFH, nondeletion type G
142270	Hereditary persistence of fetal hemoglobin
142470	[Hereditary persistence of fetal hemoglobin, heterocellular]
142857	Pemphigoid, susceptibility to
142858	Beryllium disease, chronic, susceptibility to
142959	Hand-foot-uterus syndrome, 140000
143890	Hypercholesterolemia, familial
144200	Epidermolytic palmoplantar keratoderma
145001	Hyperparathyroidism-jaw tumor syndrome
145260	Pseudohypoaldosteronism, type II
145410	Opitz G syndrome, type II
145981	Hypocalciuric hypercalcemia, type II
146760	[IgG receptor I, phagocytic, familial deficiency of]
146790	Lupus nephritis, susceptibility to
147050	Atopy
147141	Leukemia, acute lymphoblastic
147200	[Kappa light chain deficiency]
147440	Growth retardation with deafness and mental retardation
147670	Rabson-Mendenhall syndrome
147670	Diabetes mellitus, insulin-resistant, with acanthosis nigricans
147670	Leprechaunism
148065	White sponge nevus, 193900
148066	Epidermolysis bullosa simplex, Koebner, Dowling-Meara, and
	Weber-Cockayne types, 131900, 131760, 131800
148066	Epidermolysis bullosa simplex, recessive, 601001
148067	Nonepidermolytic palmoplantar keratoderma, 600962
148067	Pachyonychia congenita, Jadassohn-Lewandowsky type, 167200
148069	Pachyonychia congenita, Jackson-Lawler type, 167210
148080	Epidermolytic hyperkeratosis, 113800
150270	Laryngeal adductor paralysis
151400	Leukemia/lymphoma, B-cell, 1
151440	Leukemia, T-cell acute lymphoblastoid
151670	Hepatic lipase deficiency
152200	Coronary artery disease, susceptibility to
152445	Vohwinkel syndrome, 124500
152445	Erythrokeratoderma, progressive symmetric, 602036
152760	Hypogonadotropic hypogonadism due to GNRH deficiency, 227200
152790	Precocious puberty, male, 176410
152790	Leydig cell hypoplasia
153700	Macular dystrophy, vitelliform type
153880	Macular dystrophy, dominant cystoid

154275	Malignant hyperthermia susceptibility 2
154276	Malignant hyperthermia susceptibility 3
155555	[Red hair/fair skin]
155555	UV-induced skin damage, vulnerability to
156225	Muscular dystrophy, congenital merosin-deficient
156850	Cataract, congenital, with microphthalmia
157170	Holoprosencephaly-2
158590	Spinal muscular atrophy-4
159001	Muscular dystrophy, limb-girdle, type 1B
160781	Cardiomyopathy, hypertrophic, mid-left ventricular chamber type
160900	Myotonic dystrophy
161015	Mitochondrial complex I deficiency, 252010
163950	Noonan syndrome-1
163950	Cardiofaciocutaneous syndrome, 115150
164009	Leukemia, acute promyelocytic, NUMA/RARA type
164200	Oculodentodigital dysplasia
164200	Syndactyly, type III, 186100
164731	Ovarian carcinoma, 167000
164953	Liposarcoma
166600	Osteopetrosis, AD, type II
167000	Ovarian cancer, serous
167250	Paget disease of bone
168461	Multiple myeloma, 254250
168461	Parathyroid adenomatosis 1
168461	Centrocytic lymphoma
168468	Metaphyseal chondrodysplasia, Murk Jansen type, 156400
168500	Parietal foramina
168610	Parkinsonism-dementia with pallidopontonigral degeneration
170261	Bare lymphocyte syndrome, type I, due to TAP2 deficiency
170995	Zellweger syndrome-2
171190	Hypertension, essential, 145500
171650	Lysosomal acid phosphatase deficiency
172400	Hemolytic anemia due to glucosephosphate isomerase deficiency
172400	Hydrops fetalis, one form
173360	Thrombophilia due to excessive plasminogen activator inhibitor
173360	Hemorrhagic diathesis due to PAI1 deficiency
173370	Plasminogen activator deficiency
173850	Polio, susceptibility to
173870	Xeroderma pigmentosum
173870	Fanconi anemia
174000	Medullary cystic kidney disease, AD
176705	Breast cancer, sporadic
176730	Diabetes mellitus, rare form
176730	Hyperproinsulinemia, familial
176730	MODY, one form
	<u></u>

176930	Dysprothrombinemia
176930	Hypoprothrombinemia
177900	Psoriasis susceptibility-1
178640	Pulmonary alveolar proteinosis, congenital, 265120
179450	Ragweed sensitivity
179605	Retinitis pigmentosa, digenic
179605	Retinitis pigmentosa-7, peripherin-related
179605	Retinitis punctata albescens
179605	Butterfly dystrophy, retinal
179605	Macular dystrophy
179755	Renal cell carcinoma, papillary, 1
180020	Retinal cone dystrophy-1
180100	Retinitis pigmentosa-1
180104	Retinitis pigmentosa-9
180297	Anemia, hemolytic, Rh-null, suppressor type, 268150
180721	Retinitis pigmentosa, digenic
180840	Susceptibility to IDDM
180901	Malignant hyperthermia susceptibility 1, 145600
180901	Central core disease, 117000
181430	Scapuloperoneal syndrome, myopathic type
182280	Small-cell cancer of lung
182380	Glucose/galactose malabsorption
182601	Spastic paraplegia-4
182860	Pyropoikilocytosis
182860	Spherocytosis, recessive
182860	Elliptocytosis-2
182900	Spherocytosis-2
185430	Atherosclerosis, susceptibility to
185800	Symphalangism, proximal
186580	Arthrocutaneouveal granulomatosis
186855	Leukemia-2, T-cell acute lymphoblastic
188070	Bleeding disorder due to defective thromboxane A2 receptor
188540	Hypothyroidism, nongoitrous
188826	Sorsby fundus dystrophy, 136900
189800	Preeclampsia/eclampsia
190020	Bladder cancer, 109800
190040	Dermatofibrosarcoma protuberans
190040	Giant-cell fibroblastoma
190040	Meningioma, SIS-related
190182	Colon cancer
190182	Colorectal cancer, familial nonpolyposis, type 6
190198	Leukemia, T-cell acute lymphoblastic
191092	Tuberous sclerosis-2
191100	Tuberous sclerosis-1
191170	Colorectal cancer, 114500
	Coloroctal Callott, 114300

191170	Li-Fraumeni syndrome
191181	Cervical carcinoma
191290	
191315	Segawa syndrome, recessive
192500	Insensitivity to pain, congenital, with anhidrosis, 256800
	Jervell and Lange-Nielsen syndrome, 220400
192500	Long QT syndrome-1
193235	Vitreoretinopathy, neovascular inflammatory
193500	Rhabdomyosarcoma, alveolar, 268220
193500	Waardenburg syndrome, type I
193500	Waardenburg syndrome, type III, 148820
193500	Craniofacial-deafness-hand syndrome, 122880
194071	Wilms tumor, type 2
194071	Adrenocortical carcinoma, hereditary, 202300
200350	Acetyl-CoA carboxylase deficiency
201460	Acyl-CoA dehydrogenase, long chain, deficiency of
201910	Adrenal hyperplasia, congenital, due to 21-hydroxylase deficiency
204500	Ceroid-lipofuscinosis, neuronal 2, classic late infantile
205100	Amyotrophic lateral sclerosis, juvenile
207750	Hyperlipoproteinemia, type Ib
209901	Bardet-Biedl syndrome 1
215700	Citrullinemia
216900	Achromatopsia
217000	C2 deficiency
217050	C6 deficiency
217050	Combined C6/C7 deficiency
217070	C7 deficiency
221770	Polycystic lipomembranous osteodysplasia with sclerosing
	leukencephalopathy
221820	Gliosis, familial progressive subcortical
222100	Diabetes mellitus, insulin-dependent-1
223360	Dopamine-beta-hydroxylase deficiency
223900	Dysautonomia, familial
227646	Fanconi anemia, type D
227650	Fanconi anemia, type A
230400	Galactosemia
230450	Hemolytic anemia due to gamma-glutamylcysteine synthetase
	deficiency
230800	Gaucher disease
230800	Gaucher disease with cardiovascular calcification
231670	Glutaricaciduria, type I
231680	Glutaricaciduria, type IIA
231950	Glutathioninuria
232200	Glycogen storage disease I
232400	Glycogen storage disease IIIa
232400	Glycogen storage disease IIIb
	Cryoogen storage disease into

232600	McArdle disease
232800	Glycogen storage disease VII
233100	[Renal glucosuria]
235200	Hemochromatosis
237300	Carbamoylphosphate synthetase I deficiency
239500	Hyperprolinemia, type I
245050	Ketoacidosis due to SCOT deficiency
247200	Miller-Dieker lissencephaly syndrome
248600	Maple syrup urine disease, type Ia
248611	Maple syrup urine disease, type Ib
249000	Meckel syndrome
250250	Cartilage-hair hypoplasia
251170	Mevalonicaciduria
252920	Sanfilippo syndrome, type B
253000	Mucopolysaccharidosis IVA
253250	Mulibrey nanism
253700	Muscular dystrophy, limb-girdle, type 2C
253800	Walker-Warburg syndrome, 236670
253800	Fukuyama type congenital muscular dystrophy
256540	Galactosialidosis
256550	Sialidosis, type I
256550	Sialidosis, type II
256850	Giant axonal neuropathy-1
258501	3-methylglutaconicaciduria, type III
259700	Osteopetrosis, recessive
259770	Osteoporosis-pseudoglioma syndrome
261510	Pseudo-Zellweger syndrome
262000	Bjornstad syndrome
263200	Polycystic kidney disease, autosomal recessive
266200	Anemia, hemolytic, due to PK deficiency
268900	[Sarcosinemia]
270800	Spastic paraplegia-5A
272800	Tay-Sachs disease
272800	[Hex A pseudodeficiency]
272800	GM2-gangliosidosis, juvenile, adult
275350	Transcobalamin II deficiency
276700	Tyrosinemia, type I
276710	Tyrosinemia, type III
277700	Werner syndrome
278300	Xanthinuria, type I
278700	Xeroderma pigmentosum, group A
300000	Opitz G syndrome, type I
300066	Deafness, X-linked 6, sensorineural
300067	Subcortical laminar heterotopia, X-linked dominant
300067	Lissencephaly, X-linked

200077	
300077	Mental retardation, X-linked 29
300121	Subcortical laminal heteropia, X-linked, 300067
300121	Lissencephaly, X-linked, 300067
300123	Mental retardation with isolated growth hormone deficiency
300310	Agammaglobulinemia, type 2, X-linked
300500	Ocular albinism, Nettleship-Falls type
300650	Ocular albinism with sensorineural deafness
301200	Amelogenesis imperfecta
301201	Amelogenesis imperfecta-3, hypoplastic type
301220	Partington syndrome II
301835	Arts syndrome
301845	Bazex syndrome
301900	Borjeson-Forssman-Lehmann syndrome
302350	Nance-Horan syndrome
302950	Chondrodysplasia punctata, X-linked recessive, 302940
304050	Aicardi syndrome
304110	Craniofrontonasal dysplasia
304340	Mental retardation, X-linked, syndromic-5, with Dandy-Walker
•	malformation, basal ganglia disease, and seizures
306100	Gonadal dysgenesis, XY female type
307150	Hypertrichosis, congenital generalized
307700	Hypoparathyroidism, X-linked
308000	HPRT-related gout
308000	Lesch-Nyhan syndrome
308700	Kallmann syndrome
309000	Lowe syndrome
309530	Mental retardation, X-linked 1, non-dysmorphic
309585	Mental retardation, X-linked, syndromic-6, with gynecomastia and
	obesity
310490	Cowchock syndrome
311200	Oral-facial-digital syndrome 1
311850	Phosphoribosyl pyrophosphate synthetase-related gout
312040	N syndrome, 310465
313850	Thoracoabdominal syndrome
600040	Colorectal cancer
600045	Xeroderma pigmentosum, group E, subtype 2
600059	Retinitis pigmentosa-13
600105	Retinitis pigmentosa-12, autosomal recessive
600119	Muscular dystrophy, Duchenne-like, type 2
600119	Adhalinopathy, primary
600140	Rubenstein-Taybi syndrome, 180849
600163	Long QT syndrome-3
600175	Spinal muscular atrophy, congenital nonprogressive, of lower limbs
600202	Dyslexia, specific, 2
600234	HMG-CoA synthease-2 deficiency

600261	Ehlers-Danlos-like syndrome
600266	Resistance/susceptibility to TB, etc.
600273	Polycystic kidney disease, infantile severe, with tuberous sclerosis
600276	Cerebral arteriopathy with subcortical infarcts and
	leukoencephalopathy, 125310
600281	Non-insulin-dependent diabetes mellitus, 125853
600281	MODY, type 1, 125850
600309	Atrioventricular canal defect-1
600319	Diabetes mellitus, insulin-dependent, 4
600320	Insulin-dependent diabetes mellitus-5
600364	Cone dystrophy-3, 602093
600374	Bardet-Biedl syndrome 4
600528	CPT deficiency, hepatic, type I, 255120
600617	Lipoid adrenal hyperplasia, 201710
600623	Prostate cancer, 176807
600759	Alzheimer disease-4
600808	Enuresis, nocturnal, 2
600811	Xeroderma pigmentosum, group E, DDB-negative subtype, 278740
600837	Hirschsprung disease, 142623
600839	Bartter syndrome, 241200
600850	Schizophrenia disorder-4
600856	Beckwith-Wiedemann syndrome, 130650
600883	Diabetes mellitus, insulin-dependent, 8
600897	Cataract, zonular pulverulent-1, 116200
600918	Cystinuria, type III
600946	Short stature, autosomal dominant, with normal serum growth
	hormone binding protein
600946	Short stature, idiopathic
600946	Laron dwarfism, 262500
600957	Persistent Mullerian duct syndrome, type I, 261550
600958	Cardiomyopathy, familial hypertrophic, 4, 115197
600964	Refsum disease, adult, with increased pipecolicacidemia
600983	Pseudohypoaldosteronism type I, autosomal dominant, 177735
600994	Deafness, autosomal dominant 5
600996	Arrhythmogenic right ventricular dysplasia-2
601071	Deafness, autosomal recessive 9
601105	Pycnodysostosis, 265800
601154	Cardiomyopathy, dilated, 1E
601238	Cerebellar ataxia, Cayman type
601277	Ichthyosis, lamellar, type 2
601284	Hereditary hemorrhagic telangiectasia-2, 600376
601313	Polycystic kidney disease, adult type I, 173900
601316	Deafness, autosomal dominant 10
601362	DiGeorge syndrome/velocardiofacial syndrome complex-2
601363	Wilms tumor, type 4

601410	15:14
601410	Diabetes mellitus, transient neonatal
601412	Deafness, autosomal dominant 7
601414	Retinitis pigmentosa-18
601498	Peroxisomal biogenesis disorder, complementation group 4
601517	Spinocerebellar ataxia-2, 183090
601545	Lissencephaly-1
601649	Blepharophimosis, epicanthus inversus, and ptosis, type 2
601652	Glaucoma 1A, primary open angle, juvenile-onset, 137750
601666	Insulin-dependent diabetes mellitus-15
601669	Hirschsprung disease, one form
601680	Distal arthrogryposis, type 2B
601690	Platelet-activating factor acetylhydrolase deficiency
601691	Retinitis pigmentosa-19, 601718
601691	Stargardt disease-1, 248200
601691	Cone-rod dystrophy 3
601691	Fundus flavimaculatus with macular dystrophy, 248200
601718	Retinitis pigmentosa-19
601744	Systemic lupus erythematosus, susceptibility to, 1
601757	Rhizomelic chondrodysplasia punctata, type 1, 215100
601769	Osteoporosis, involutional
601769	Rickets, vitamin D-resistant, 277440
601771	Glaucoma 3A, primary infantile, 231300
601780	Ceroid-lipofuscinosis, neuronal-6, variant late infantile
601785	Carbohydrate-deficient glycoprotein syndrome, type I, 212065
601843	Hypothyroidism, congenital, 274400
601844	Pseudohypoaldosteronism type II
601846	Muscular dystrophy with rimmed vacuoles
601850	Retinitis pigmentosa-deafness syndrome
601863	Bare lymphocyte syndrome, complementation group C
601868	Deafness, autosomal dominant 13
601884	[High bone mass]
601885	Cataract, zonular pulverulent-2
601975	Ectodermal dysplasia/skin fragility syndrome
602025	Obesity/hyperinsulinism, susceptibility to
602026	Refsum disease, 266500
602078	Fibrosis of extraocular muscles, congenital, 2
602088	Nephronophthisis, infantile
602094	Lipodystrophy, familial partial
602099	Amytrophic lateral sclerosis-5
602116	Glioma
602134	Tremor, familial essential, 2
602136	Refsum disease, infantile, 266510
602136	Zellweger syndrome-1, 214100
602136	Adrenoleukodystrophy, neonatal, 202370
602216	Peutz-Jeghers syndrome, 175200

602221	Stem-cell leukemia/lymphoma syndrome
602225	Cone-rod retinal dystrophy-2, 120970
602225	Leber congenital amaurosis, type III
602229	Waardenburg-Shah syndrome, 277580
602235	Epilepsy, benign, neonatal, type 1, 121200
602280	Retinitis pigmentosa-14, 600132
602447	Coronary artery disease, susceptibility to
602475	Ossification of posterior longitudinal ligament of spine
602477	Febrile convulsions, familial, 2
602491	Hyperlipidemia, familial combined, 1
602544	Parkinson disease, juvenile, type 2, 600116
602631	Rhabdomyosarcoma, 268210
602631	Breast Cancer
602716	Nephrosis-1, congenital, Finnish type, 256300
602772	Retinitis pitmentosa-24
602782	Faisalabad histiocytosis
602783	Spastic paraplegia-7

## Polynucleotide and Polypeptide Variants

[0113] The present invention is also directed to variants of the reproductive system associated polynucleotide sequence disclosed in SEQ ID NO:X or the complementary strand thereto, nucleotide sequences encoding the polypeptide of SEQ ID NO:Y, the nucleotide sequence of SEQ ID NO:X encoding the polypeptide sequence as defined in column 6 of Table 1A, nucleotide sequences encoding the polypeptide as defined in column 6 of Table 1A, the nucleotide sequence as defined in columns 8 and 9 of Table 2, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in column 6 of Table 1B, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in column 6 of Table 1B, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in column 6 of Table 1B, the cDNA sequence contained in Clone ID NO:Z, and/or nucleotide sequences encoding a polypeptide encoded by the cDNA sequence contained in Clone ID NO:Z.

[0114] The present invention also encompasses variants of the polypeptide sequence disclosed in SEQ ID NO:Y, a polypeptide sequence as defined in column 6 of Table 1A, a polypeptide sequence encoded by the polynucleotide sequence in SEQ

ID NO:X, a polypeptide sequence encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2, a polypeptide sequence encoded by the nucleotide sequence as defined in column 6 of Table 1B, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, and/or a polypeptide sequence encoded by the cDNA sequence contained in Clone ID NO:Z.

[0115] "Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

Thus, one aspect of the invention provides an isolated nucleic acid [0116] molecule comprising, or alternatively consisting of, a polynucleotide having a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence described in SEQ ID NO:X or contained in the cDNA sequence of Clone ID NO:Z; (b) a nucleotide sequence in SEQ ID NO:X or the cDNA in Clone ID NO:Z which encodes a mature reproductive system associated polypeptide; (c) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of Clone ID NO:Z, which encodes a biologically active fragment of a reproductive system associated polypeptide; (d) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of Clone ID NO:Z, which encodes an antigenic fragment of a reproductive system associated polypeptide; (e) a nucleotide sequence encoding a reproductive system associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (f) a nucleotide sequence encoding a mature reproductive system associated polypeptide of the amino acid sequence of SEQ ID NO:Y or the amino acid sequence encoded by the cDNA in Clone ID NO:Z; (g) a nucleotide sequence encoding a biologically active fragment of a reproductive system associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (h) a nucleotide sequence encoding an antigenic fragment of a reproductive system associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; and (i) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), or (h), above.

[0117] The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), or (i) above, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence of the cDNA contained in Clone ID NO:Z or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide sequence encoded by the nucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA contained in Clone ID NO:Z, the nucleotide coding sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, a nucleotide sequence encoding the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, the nucleotide coding sequence in SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto, a nucleotide sequence encoding the polypeptide encoded by the nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto, the nucleotide sequence in SEQ ID NO:X encoding the polypeptide sequence as defined in column 6 of Table 1A or the complementary strand thereto, nucleotide sequences encoding a polypeptide as defined in column 6 of Table 1A or the complementary strand thereto, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides and nucleic acids.

[0118] In a preferred embodiment, the invention encompasses nucleic acid molecules which comprise, or alternatively, consist of a polynucleotide which hybridizes under stringent hybridization conditions, or alternatively, under lower stringency conditions, to a polynucleotide in (a), (b), (c), (d), (e), (f), (g), (h), or (i) above, as are polypeptides encoded by these polynucleotides. In another preferred

embodiment, polynucleotides which hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

[0119] In another embodiment, the invention provides a purified protein comprising, or alternatively consisting of, a polypeptide having an amino acid sequence selected from the group consisting of: (a) the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (b) the amino acid sequence of a mature reproductive system associated polypeptide having the amino acid sequence of SEQ ID NO:Y or the amino acid sequence encoded by the cDNA in Clone ID NO:Z; (c) the amino acid sequence of a biologically active fragment of a reproductive system associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence of an antigenic fragment of a reproductive system associated polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Y.

[0120] The present invention is also directed to proteins which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the amino acid sequences in (a), (b), (c), or (d), above, the amino acid sequence shown in SEQ ID NO:Y, the amino acid sequence encoded by the cDNA contained in Clone ID NO:Z, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B, the amino acid sequence as defined in column 6 of Table 1A, an amino acid sequence encoded by the nucleotide sequence in SEQ ID NO:X, and an amino acid sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X. Fragments of these polypeptides are also provided (e.g., those fragments described herein). Further proteins encoded by polynucleotides which hybridize to the complement of the nucleic acid molecules encoding these amino acid sequences under stringent hybridization conditions or alternatively, under lower

stringency conditions, are also encompassed by the invention, as are the polynucleotides encoding these proteins.

- "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence referred to in Table 1A or 2 as the ORF (open reading frame), or any fragment specified, as described herein.
- As a practical matter, whether any particular nucleic acid molecule or [0122]polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is expressed as percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.
- [0123] If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3'

truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query [0124] sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

[0125] By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other

words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 80%, [0126] 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence of a polypeptide referred to in Table 1A (e.g., an amino acid sequence identified in columns 5 or 6) or Table 2 (e.g., the amino acid sequence of the polypeptide encoded by the polynucleotide sequence defined in columns 8 and 9 of Table 2) or a fragment thereof, the amino acid sequence of the polypeptide encoded by the polynucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B or a fragment thereof, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X or a fragment thereof, or an amino acid sequence of the polypeptide encoded by cDNA contained in Clone ID NO:Z, or a fragment thereof, can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci.6:237-245 (1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is expressed as percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

[0127] If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N-

and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C- terminal residues of the subject sequence.

[0128]For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

[0129] The polynucleotide variants of the invention may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide

variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, polypeptide variants in which less than 50, less than 40, less than 30, less than 20, less than 10, or 5-50, 5-25, 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

- [0130] Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.
- [0131] Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the polypeptides of the present invention without substantial loss of biological function. As an example, the authors of Ron et al., J. Biol. Chem. 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)
- [0132] Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem. 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the

molecule could be altered with little effect on either [binding or biological activity]." In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

[0134] Thus, the invention further includes polypeptide variants which show a functional activity (e.g., biological activity) of the polypeptides of the invention. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity.

[0135]The present application is directed to nucleic acid molecules at least 80%. 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, (e.g., encoding a polypeptide having the amino acid sequence of an N and/or C terminal deletion), irrespective of whether they encode a polypeptide having functional activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having functional activity include, inter alia, (1) isolating a gene or allelic or splice variants thereof in a cDNA library; (2) in situ hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the gene, as described in Verma et al., Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York (1988); (3) Northern Blot analysis for detecting mRNA expression in specific tissues (e.g., normal reproductive system tissues or diseased

reproductive system tissues); and (4) in situ hybridization (e.g., histochemistry) for detecting mRNA expression in specific tissues (e.g., normal reproductive system tissues or diseased reproductive system tissues).

[0136] Preferred, however, are nucleic acid molecules having sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, which do, in fact, encode a polypeptide having functional activity. By a polypeptide having "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide of the invention for binding) to an anti-polypeptide of the invention antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention.

[0137] The functional activity of the polypeptides, and fragments, variants and derivatives of the invention, can be assayed by various methods.

For example, in one embodiment where one is assaying for the ability to [0138] bind or compete with full-length polypeptide of the present invention for binding to an anti-polypeptide of the invention antibody, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

[0139] In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky et al., Microbiol. Rev. 59:94-123 (1995). In another embodiment, the ability of physiological correlates of a polypeptide of the present invention to bind to a substrate(s) of the polypeptide of the invention can be routinely assayed using techniques known in the art.

- [0140] In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present invention and fragments, variants and derivatives thereof to elicit polypeptide related biological activity (either *in vitro* or *in vivo*). Other methods will be known to the skilled artisan and are within the scope of the invention.
- [0141] Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to, for example, the nucleic acid sequence of the cDNA contained in Clone ID NO:Z, a nucleic acid sequence referred to in Table 1A (e.g., SEQ ID NO:X), a nucleic acid sequence disclosed in Table 2 (e.g., the nucleic acid sequence delineated in columns 8 and 9) or fragments thereof, will encode polypeptides "having functional activity." In fact, since degenerate variants of any of these nucleotide sequences all encode the same polypeptide, in many instances, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.
- [0142] For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," Science 247:1306-1310

(1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

- [0143] The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.
- [0144] The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. See Cunningham et al., Science 244:1081-1085 (1989). The resulting mutant molecules can then be tested for biological activity.
- [0145] As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly. Besides conservative amino acid substitutions, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitutions with one or more of the amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example,

polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, serum albumin (preferably human serum albumin) or a fragment or variant thereof, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

- [0146] For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. See Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).
- [0147] A further embodiment of the invention relates to polypeptides which comprise the amino acid sequence of a polypeptide having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions from a polypeptide sequence disclosed herein. Of course it is highly preferable for a polypeptide to have an amino acid sequence which comprises the amino acid sequence of a polypeptide of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, an amino acid sequence encoded by the complement of SEQ ID NO:X, and/or the amino acid sequence encoded by cDNA contained in Clone ID NO:Z which contains, in order of ever-increasing preference, at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid substitutions.
- In specific embodiments, the polypeptides of the invention comprise, or alternatively, consist of, fragments or variants of a reference amino acid sequence selected from: (a) the amino acid sequence of SEQ ID NO:Y or fragments thereof (e.g., the mature form and/or other fragments described herein); (b) the amino acid sequence encoded by SEQ ID NO:X or fragments thereof; (c) the amino acid sequence encoded by the complement of SEQ ID NO:X or fragments thereof; (d) the amino acid

sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or fragments thereof; and (e) the amino acid sequence encoded by cDNA contained in Clone ID NO:Z or fragments thereof; wherein the fragments or variants have 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, amino acid residue additions, substitutions, and/or deletions when compared to the reference amino acid sequence. In preferred embodiments, the amino acid substitutions are conservative. Polynucleotides encoding these polypeptides are also encompassed by the invention.

## Polynucleotide and Polypeptide Fragments

The present invention is also directed to polynucleotide fragments of the [0149] polynucleotides (nucleic acids) of the invention. In the present invention, a "polynucleotide fragment" refers to a polynucleotide having a nucleic acid sequence which, for example: is a portion of the cDNA contained in Clone ID NO:Z or the complementary strand thereto; is a portion of the polynucleotide sequence encoding the polypeptide encoded by the cDNA contained in Clone ID NO:Z or the complementary strand thereto; is a portion of a polynucleotide sequence encoding the amino acid sequence encoded by the region of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the polynucleotide sequence of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the polynucleotide sequence in SEO ID NO:X or the complementary strand thereto; is a polynucleotide sequence encoding a portion of the polypeptide of SEQ ID NO:Y; is a polynucleotide sequence encoding a portion of a polypeptide encoded by SEQ ID NO:X; is a polynucleotide sequence encoding a portion of a polypeptide encoded by the complement of the polynucleotide sequence in SEQ ID NO:X; is a portion of a polynucleotide sequence encoding the amino acid sequence encoded by the region of SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto; or is a portion of the polynucleotide sequence of SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto.

[0150] The polynucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75

nt, or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in Clone ID NO:Z, or the nucleotide sequence shown in SEQ ID NO:X or the complementary stand thereto. In this context "about" includes the particularly recited value or a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., at least 160, 170, 180, 190, 200, 250, 500, 600, 1000, or 2000 nucleotides in length) are also encompassed by the invention.

Moreover, representative examples of polynucleotide fragments of the [0151] invention, comprise, or alternatively consist of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of SEQ ID NO:X, or the complementary strand

thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

Further representative examples of polynucleotide fragments of the [0152] invention, comprise, or alternatively consist of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of the cDNA sequence contained in Clone ID NO:Z, or the complementary strand thereto. In this context "about" includes the

particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

[0153] Moreover, representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a nucleic acid sequence comprising one, two, three, four, five, six, seven, eight, nine, ten, or more of the above described polynucleotide fragments of the invention in combination with a polynucleotide sequence delineated in Table 1B column 6. Additional, representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a nucleic acid sequence comprising one, two, three, four, five, six, seven, eight, nine, ten, or more of the above described polynucleotide fragments of the invention in combination with a polynucleotide sequence that is the complementary strand of a sequence delineated in column 6 of Table 1B. In further embodiments, the abovedescribed polynucleotide fragments of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the abovedescribed polynucleotide fragments of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also

encompassed by the invention. Additionally, fragments and variants of the abovedescribed polynucleotides and polypeptides are also encompassed by the invention.

- [0154] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1B, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.
- [0155] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.
- [0156] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in the same row of column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.
- [0157] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that

encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0158] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X (e.g., as described herein) are directly contiguous Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0159] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0160] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 are directly contiguous. In preferred

embodiments, the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B is directly contiguous with the 5' 10 polynucleotides of the next sequential exon delineated in Table 1B, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[0161] In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y, a portion of an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, a portion of an amino acid sequence encoded by the polynucleotide sequence of SEQ ID NO:X, a portion of an amino acid sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, and/or a portion of an amino acid sequence encoded by the cDNA contained in Clone ID NO:Z. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320. 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region. In a preferred embodiment, polypeptide fragments of the invention include, for example, fragments comprising, or alternatively consisting

of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region of SEQ ID NO:Y. Moreover, polypeptide fragments of the invention may be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, or ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

[0162] Even if deletion of one or more amino acids from the N-terminus of a protein results in modification of loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example, the ability of shortened muteins to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptides generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the N-terminus. Whether a particular polypeptide lacking N-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted N-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

[0163] Accordingly, polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or

the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions is preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

The present invention further provides polypeptides having one or more residues deleted from the amino terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X or the complement thereof, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, a polypeptide encoded by the portion of SEQ ID NO:B as defined in column 6 of Table 1B, and/or a polypeptide encoded by the cDNA contained in Clone ID NO:Z). In particular, N-terminal deletions may be described by the general formula m-q, where q is a whole integer representing the total number of amino acid residues in a polypeptide of the invention (e.g., the polypeptide disclosed in SEQ ID NO:Y, or the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2), and m is defined as any integer ranging from 2 to q-6. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The present invention further provides polypeptides having one or more residues from the carboxy terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or a polypeptide encoded by the cDNA contained in Clone ID NO:Z). In particular, C-terminal deletions may be described by the general formula 1-n, where n is any whole integer ranging from 6 to q-1, and where n corresponds to the position of amino acid residue in a polypeptide of the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0166] In addition, any of the above described N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also

provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of a polypeptide encoded by SEQ ID NO:X (e.g., including, but not limited to, the preferred polypeptide disclosed as SEQ ID NO:Y and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2), the cDNA contained in Clone ID NO:Z, and/or the complement thereof, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification of loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example the ability of the shortened mutein to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

[0168] The present application is also directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence set forth herein. In preferred embodiments, the application is directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to polypeptides having the amino acid sequence of the specific N- and C-terminal deletions. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0169] Any polypeptide sequence encoded by, for example, the polynucleotide sequences set forth as SEQ ID NO:X or the complement thereof, (presented, for example, in Tables 1A and 2), the cDNA contained in Clone ID NO:Z, or the polynucleotide sequence as defined in column 6 of Table 1B, may be analyzed to

determine certain preferred regions of the polypeptide. For example, the amino acid sequence of a polypeptide encoded by a polynucleotide sequence of SEQ ID NO:X (e.g., the polypeptide of SEQ ID NO:Y and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2) or the cDNA contained in Clone ID NO:Z may be analyzed using the default parameters of the DNASTAR computer algorithm (DNASTAR, Inc., 1228 S. Park St., Madison, WI 53715 USA; http://www.dnastar.com/).

- [0170] Polypeptide regions that may be routinely obtained using the DNASTAR computer algorithm include, but are not limited to, Garnier-Robson alpha-regions, beta-regions, turn-regions, and coil-regions; Chou-Fasman alpha-regions, beta-regions, and turn-regions; Kyte-Doolittle hydrophilic regions and hydrophobic regions; Eisenberg alpha- and beta-amphipathic regions; Karplus-Schulz flexible regions; Emini surface-forming regions; and Jameson-Wolf regions of high antigenic index. Among highly preferred polynucleotides of the invention in this regard are those that encode polypeptides comprising regions that combine several structural features, such as several (e.g., 1, 2, 3 or 4) of the features set out above.
- [0171] Additionally, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Emini surface-forming regions, and Jameson-Wolf regions of high antigenic index (i.e., containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) can routinely be used to determine polypeptide regions that exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from data by DNASTAR analysis by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.
- [0172] Preferred polypeptide fragments of the invention are fragments comprising, or alternatively, consisting of, an amino acid sequence that displays a functional activity (e.g. biological activity) of the polypeptide sequence of which the amino acid sequence is a fragment. By a polypeptide displaying a "functional activity" is meant a polypeptide capable of one or more known functional activities associated with a full-

length protein, such as, for example, biological activity, antigenicity, immunogenicity, and/or multimerization, as described herein.

[0173] Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

[0174] In preferred embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the antigenic fragments of the polypeptide of SEQ ID NO:Y, or portions thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The present invention encompasses polypeptides comprising, or [0175]alternatively consisting of, an epitope of: the polypeptide sequence shown in SEQ ID NO:Y; a polypeptide sequence encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2; the polypeptide sequence encoded by the portion of SEQ ID NO:B as defined in column 6 of Table 1B or the complement thereto; the polypeptide sequence encoded by the cDNA contained in Clone ID NO:Z; or the polypeptide sequence encoded by a polynucleotide that hybridizes to the sequence of SEQ ID NO:X, the complement of the sequence of SEQ ID NO:X, the complement of a portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, or the cDNA sequence contained in Clone ID NO:Z under stringent hybridization conditions or alternatively, under lower stringency hybridization as defined supra. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X, or a fragment thereof), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to the complementary strand under stringent hybridization conditions or alternatively, under lower stringency hybridization conditions defined supra.

[0176] The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and

most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies described *infra*. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross- reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

- [0177] Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)
- In the present invention, antigenic epitopes preferably contain a sequence 101781 of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).
- [0179] Non-limiting examples of epitopes of polypeptides that can be used to generate antibodies of the invention include a polypeptide comprising, or alternatively consisting of, at least one, two, three, four, five, six or more of the portion(s) of SEQ

ID NO:Y specified in column 6 of Table 1A. These polypeptide fragments have been determined to bear antigenic epitopes of the proteins of the invention by the analysis of the Jameson-Wolf antigenic index which is included in the DNAStar suite of computer programs. By "comprise" it is intended that a polypeptide contains at least one, two, three, four, five, six or more of the portion(s) of SEQ ID NO:Y shown in column 6 of Table 1A, but it may contain additional flanking residues on either the amino or carboxyl termini of the recited portion. Such additional flanking sequences are preferably sequences naturally found adjacent to the portion; i.e., contiguous sequence shown in SEQ ID NO:Y. The flanking sequence may, however, be sequences from a heterologous polypeptide, such as from another protein described herein or from a heterologous polypeptide not described herein. In particular embodiments, epitope portions of a polypeptide of the invention comprise one, two, three, or more of the portions of SEQ ID NO:Y shown in column 6 of Table 1A. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[0180] Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol. 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

[0181] Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, in vivo immunization, in vitro immunization, and phage display methods. See, e.g., Sutcliffe et al., supra; Wilson et al., supra, and Bittle et al., J. Gen. Virol., 66:2347-2354 (1985). If in vivo immunization is used, animals may be immunized

with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 µg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

As one of skill in the art will appreciate, and as discussed above, the [0182] polypeptides of the present invention (e.g., those comprising an immunogenic or antigenic epitope) can be fused to heterologous polypeptide sequences. For example, polypeptides of the present invention (including fragments or variants thereof), may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof, resulting in chimeric polypeptides. By way of another non-limiting example, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused with albumin (including but not limited to recombinant human serum albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). In a preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with the mature form of human serum albumin (i.e., amino acids 1 - 585 of human serum albumin as shown in Figures 1 and 2 of EP Patent 0 322 094) which is herein incorporated by reference in its entirety. In another preferred

embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with polypeptide fragments comprising, or alternatively consisting of, amino acid residues 1-z of human serum albumin, where z is an integer from 369 to 419, as described in U.S. Patent 5,766,883 herein incorporated by reference in its entirety. Polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused to either the N- or C-terminal end of the heterologous protein (e.g., immunoglobulin Fc polypeptide or human serum albumin polypeptide). Polynucleotides encoding fusion proteins of the invention are also encompassed by the invention.

[0183] Such fusion proteins as those described above may facilitate purification and may increase half-life in vivo. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., Nature, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG Fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion desulfide bonds have also been found to be more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., J. Biochem., 270:3958-3964 (1995). Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin (iHAî) tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., 1991, Proc. Natl. Acad. Sci. USA 88:8972-897). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni2+ nitriloacetic acid-agarose column

and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

## Fusion Proteins

[0184] Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, polypeptides of the present invention which are shown to be secreted can be used as targeting molecules once fused to other proteins.

[0185] Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

[0186] In certain preferred embodiments, proteins of the invention are fusion proteins comprising an amino acid sequence that is an N and/or C- terminal deletion of a polypeptide of the invention. In preferred embodiments, the invention is directed to a fusion protein comprising an amino acid sequence that is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence of the invention. Polynucleotides encoding these proteins are also encompassed by the invention.

[0187] Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

[0188] As one of skill in the art will appreciate that, as discussed above, polypeptides of the present invention, and epitope-bearing fragments thereof, can be combined with heterologous polypeptide sequences. For example, the polypeptides of

the present invention may be fused with heterologous polypeptide sequences, for example, the polypeptides of the present invention may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM) or portions thereof (CH1, CH2, CH3, and any combination thereof, including both entire domains and portions thereof), or albumin (including, but not limited to, native or recombinant human albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)), resulting in chimeric For example, EP-A-O 464 533 (Canadian counterpart 2045869) polypeptides. discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties (EP-A 0232 262). Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. See, D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).

[0189] Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a polypeptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexahistidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984).)

[0190] Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling

(collectively referred to as "DNA shuffling"), briefly described below, and further described herein. DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308-13 (1998); each of these patents and publications are hereby incorporated by reference in its entirety). In a preferred embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc., of one or more heterologous molecules encoding a heterologous polypeptide.

[0191] Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

## Recombinant and Synthetic Production of Polypeptides of the Invention

- [0192] The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by synthetic and recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.
- [0193] The polynucleotides of the invention may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged *in vitro* using an appropriate packaging cell line and then transduced into host cells.
- [0194] The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to

name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

- [0195] As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance, glutamine synthase, for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in *E. coli* and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as *E. coli*, *Streptomyces* and *Salmonella typhimurium* cells; fungal cells, such as yeast cells (e.g., *Saccharomyces cerevisiae* or *Pichia pastoris* (ATCC Accession No. 201178)); insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, 293, NSO and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.
- [0196] Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlsbad, CA). Other suitable vectors will be readily apparent to the skilled artisan.
- [0197] Vectors which use glutamine synthase (GS) or DHFR as the selectable markers can be amplified in the presence of the drugs methionine sulphoximine or methotrexate, respectively. An advantage of glutamine synthase based vectors is the availability of cell lines (e.g., the murine myeloma cell line, NS0) which are glutamine

synthase negative. Glutamine synthase expression systems can also function in glutamine synthase expressing cells (e.g., Chinese Hamster Ovary (CHO) cells) by providing additional inhibitor to prevent the functioning of the endogenous gene. A glutamine synthase expression system and components thereof are detailed in PCT publications: WO87/04462; WO86/05807; WO89/01036; WO89/10404; and WO91/06657 which are hereby incorporated in their entireties by reference herein. Additionally, glutamine synthase expression vectors can be obtained from Lonza Biologics, Inc. (Portsmouth, NH). Expression and production of monoclonal antibodies using a GS expression system in murine myeloma cells is described in Bebbington et al., Bio/technology 10:169(1992) and in Biblia and Robinson Biotechnol. Prog. 11:1 (1995) which are herein incorporated by reference.

[0198] The present invention also relates to host cells containing the abovedescribed vector constructs described herein, and additionally encompasses host cells containing nucleotide sequences of the invention that are operably associated with one or more heterologous control regions (e.g., promoter and/or enhancer) using techniques known of in the art. The host cell can be a higher eukaryotic cell, such as a mammalian cell (e.g., a human derived cell), or a lower eukaryotic cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. A host strain may be chosen which modulates the expression of the inserted gene sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically engineered polypeptide may be controlled. Furthermore, different host cells have characteristics and specific mechanisms for the translational and post-translational processing and modification (e.g., phosphorylation, cleavage) of proteins. Appropriate cell lines can be chosen to ensure the desired modifications and processing of the foreign protein expressed.

[0199] Introduction of the nucleic acids and nucleic acid constructs of the invention into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular

Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

[0200] In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., reproductive system antigen coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with reproductive system associated polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous reproductive system associated polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous reproductive system associated polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent Number 5,641,670, issued June 24, 1997; International Publication Number WO 96/29411; International Publication Number WO 94/12650; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

Polypeptides of the present invention can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient,

depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

[0202] In one embodiment, the yeast Pichia pastoris is used to express polypeptides of the invention in a eukaryotic system. Pichia pastoris is a methylotrophic yeast which can metabolize methanol as its sole carbon source. A main step in the methanol metabolization pathway is the oxidation of methanol to formaldehyde using O2. This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, Pichia pastoris must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O2. Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (AOXI) is highly active. In the presence of methanol, alcohol oxidase produced from the AOX1 gene comprises up to approximately 30% of the total soluble protein in Pichia pastoris. See, Ellis, S.B., et al., Mol. Cell. Biol. 5:1111-21 (1985); Koutz, P.J, et al., Yeast 5:167-77 (1989); Tschopp, J.F., et al., Nucl. Acids Res. 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the AOX1 regulatory sequence is expressed at exceptionally high levels in Pichia yeast grown in the presence of methanol.

In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "*Pichia* Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector allows expression and secretion of a polypeptide of the invention by virtue of the strong *AOX1* promoter linked to the *Pichia pastoris* alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

[0204] Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as long as the proposed expression construct provides appropriately

located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

[0205] In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

[0206] In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983, Proteins: Structures and Molecular Principles, W.H. Freeman & Co., N.Y., and Hunkapiller et al., Nature, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide can be synthesized by use of a peptide synthesizer. Furthermore, if desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid, a-amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid, g-Abu, e-Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid,

3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoro-amino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

[0208] The invention encompasses polypeptides of the present invention which are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH<sub>4</sub>; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

[0209] Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

[0210] Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include iodine (121 I, 123 I, 125 I, 131 I), carbon (14 C), sulfur (35 S), tritium (3H), indium (111 In, 112 In, 113 In, 115 In, 115 In), technetium (99 Tc, 99 Tc), thallium (201 Ti), gallium (68 Ga, 67 Ga), palladium (103 Pd), molybdenum (99 Mo), xenon

(133Xe), fluorine (18F), 153Sm, 177Lu, 159Gd, 149Pm, 140La, 175Yb, 166Ho, 90Y, 47Sc, 186Re, 188Re, 142Pr, 105Rh, and 97Ru.

In specific embodiments, a polypeptide of the present invention or fragment or variant thereof is attached to macrocyclic chelators that associate with radiometal ions, including but not limited to, <sup>177</sup>Lu, <sup>90</sup>Y, <sup>166</sup>Ho, and <sup>153</sup>Sm, to polypeptides. In a preferred embodiment, the radiometal ion associated with the macrocyclic chelators is <sup>111</sup>In. In another preferred embodiment, the radiometal ion associated with the macrocyclic chelator is <sup>90</sup>Y. In specific embodiments, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane-N,N',N",N"'-tetraacetic acid (DOTA). In other specific embodiments, DOTA is attached to an antibody of the invention or fragment thereof via a linker molecule. Examples of linker molecules useful for conjugating DOTA to a polypeptide are commonly known in the art - see, for example, DeNardo et al., Clin Cancer Res. 4(10):2483-90 (1998); Peterson et al., Bioconjug. Chem. 10(4):553-7 (1999); and Zimmerman et al, Nucl. Med. Biol. 26(8):943-50 (1999); which are hereby incorporated by reference in their entirety.

[0212]As mentioned, the reproductive system associated proteins of the invention may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given reproductive system associated polypeptide. Reproductive system associated polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic reproductive system associated polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization,

selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth. Enzymol. 182:626-646 (1990); Rattan et al., Ann. N.Y. Acad. Sci. 663:48-62 (1992)).

[0213] Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

[0214] The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example, the polyethylene glycol may have an average molecular weight of about 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, or 100,000 kDa.

[0215] As noted above, the polyethylene glycol may have a branched structure.

Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo et al., Appl. Biochem. Biotechnol. 56:59-72 (1996); Vorobjev et al., Nucleosides Nucleotides 18:2745-2750 (1999); and Caliceti et al., Bioconjug. Chem. 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

[0216] The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, such as, for example, the method disclosed in EP 0 401 384 (coupling PEG to G-CSF), herein incorporated by reference; see also Malik et al., Exp. Hematol. 20:1028-1035 (1992), reporting pegylation of GM-CSF using tresyl chloride. For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

[0218] One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein

(polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

- [0219] As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be attached to the protein either directly or by an intervening linker. Linkerless systems for attaching polyethylene glycol to proteins are described in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992); Francis et al., Intern. J. of Hematol. 68:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated herein by reference.
- [0220] One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride (CISO<sub>2</sub>CH<sub>2</sub>CF<sub>3</sub>). Upon reaction of protein with tresylated MPEG, polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoreothane sulphonyl group.
- [0221] Polyethylene glycol can also be attached to proteins using a number of different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-

succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number of additional polyethylene glycol derivatives and reaction chemistries for attaching polyethylene glycol to proteins are described in International Publication No. WO 98/32466, the entire disclosure of which is incorporated herein by reference. Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

- The number of polyethylene glycol moieties attached to each protein of the invention (i.e., the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of substitution within ranges such as 1-3, 2-4, 3-5, 4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992).
- [0223] The reproductive system associated polypeptides of the invention can be recovered and purified from chemical synthesis and recombinant cell cultures by standard methods which include, but are not limited to, ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification. Well known techniques for refolding protein may be employed to regenerate active conformation when the polypeptide is denatured during isolation and/or purification.
- [0224] Reproductive system associated polynucleotides and polypeptides may be used in accordance with the present invention for a variety of applications, particularly those that make use of the chemical and biological properties of reproductive system associated antigens. Among these are applications in the detection, prevention, diagnosis and/or treatment of diseases associated with the reproductive system, such as e.g., cancers of the reproductive system, tumors, injuries and trauma, infections,

congenital defects, and diseases or disorders which result in infertility, complications with pregnancy, labor, or parturition, postpartum difficulties, and as listed below in the section entitled "Reproductive System Disorders". Additional applications relate to diagnosis and to treatment of disorders of cells, tissues and organisms. These aspects of the invention are discussed further below.

[0225] In a preferred embodiment, polynucleotides expressed in a particular tissue type (see, e.g., Table 1A, column 7) are used to detect, diagnose, treat, prevent and/or prognose disorders associated with the tissue type.

[0226] The polypeptides of the invention may be in monomers or multimers (i.e., dimers, trimers, tetramers and higher multimers). Accordingly, the present invention relates to monomers and multimers of the polypeptides of the invention, their preparation, and compositions (preferably, Therapeutics) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers, or at least tetramers.

Multimers encompassed by the invention may be homomers or heteromers. [0227] As used herein, the term homomer refers to a multimer containing only polypeptides corresponding to a protein of the invention (e.g., the amino acid sequence of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X or the complement of SEQ ID NO:X, the amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or an amino acid sequence encoded by cDNA contained in Clone ID NO:Z (including fragments, variants, splice variants, and fusion proteins, corresponding to these as described herein)). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid sequence. In another specific embodiment, a homomer of the invention is a multimer containing polypeptides having different amino acid sequences. In specific embodiments, the multimer of the invention is a homodimer (e.g., containing two polypeptides having identical or different amino acid sequences) or a homotrimer (e.g., containing three polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at least a homotrimer, or at least a homotetramer.

[0228] As used herein, the term heteromer refers to a multimer containing two or more heterologous polypeptides (i.e., polypeptides of different proteins) in addition to the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

Multimers of the invention may be the result of hydrophobic, hydrophilic, [0229] ionic and/or covalent associations and/or may be indirectly linked by, for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or heterotetramers, are formed when polypeptides of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence (e.g., that recited in SEQ ID NO:Y, encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or encoded by the cDNA contained in Clone ID NO:Z). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a fusion protein. In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., U.S. Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from another protein that is capable of forming covalently associated multimers, such as for example,

osteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

- [0230] Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., Science 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.
- [0231] Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (FEBS Letters 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.
- [0232] In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention containing Flag® polypeptide sequence. In a further embodiment, proteins of the

invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

[0233] The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely modified by the addition of cysteine or biotin to the C-terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the polypeptide components desired to be contained in the multimer of the invention (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

[0234] Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the invention to a sequence encoding a linker polypeptide and then further to a synthetic polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., U.S Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described

herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hydrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., U.S. Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

# **Antibodies**

Further polypeptides of the invention relate to antibodies and T-cell antigen [0235] receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of the invention (e.g., a polypeptide or fragment or variant of the amino acid sequence of SEQ ID NO:Y or a polypeptide encoded by the cDNA contained in Clone ID NO:Z, and/or an epitope, of the present invention) as determined by immunoassays well known in the art for assaying specific antibody-antigen binding. Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), intracellularly-made antibodies (i.e., intrabodies), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule. In preferred embodiments, the immunoglobulin molecules of the invention are IgG1. In other preferred embodiments, the immunoglobulin molecules of the invention are IgG4.

[0236] Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')2, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge

region, CH1, CH2, and CH3 domains. Also included in the invention are antigenbinding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, ship rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

- The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).
- of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, or by size in contiguous amino acid residues, or listed in the Tables and Figures. Preferred epitopes of the invention include those shown in column 6 of Table 1A, as well as polynucleotides that encode these epitopes. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.
- [0239] Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog, or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least

75%, at least 70%, at least 65%, at least 65%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or Kd less than 5 X 10<sup>-2</sup> M,  $10^{-2}$  M, 5 X  $10^{-3}$  M,  $10^{-3}$  M, 5 X  $10^{-4}$  M,  $10^{-4}$  M, 5 X  $10^{-5}$  M,  $10^{-5}$  M, 5 X  $10^{-6}$  M,  $10^{-6}$ M, 5 X  $10^{-7}$  M,  $10^{7}$  M, 5 X  $10^{-8}$  M,  $10^{-8}$  M, 5 X  $10^{-9}$  M,  $10^{-9}$  M, 5 X  $10^{-10}$  M,  $10^{-10}$ M, 5 X  $10^{-11}$  M,  $10^{-11}$  M, 5 X  $10^{-12}$  M,  $10^{-12}$  M, 5 X  $10^{-13}$  M,  $10^{-13}$  M, 5 X  $10^{-14}$  M,  $10^{-10}$  $^{14}$  M, 5 X  $10^{-15}$  M, or  $10^{-15}$  M.

[0240] The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herei-n. In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 50%.

[0241] Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferably, antibodies of the present invention bind

an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described *supra*). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

[0242] The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res. 58(16):3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998); Prat et al., J. Cell. Sci. 111(Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautard et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al.,

Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

[0243] Antibodies of the present invention may be used, for example, to purify, detect, and target the polypeptides of the present invention, including both in vitro and in vivo diagnostic and therapeutic methods. For example, the antibodies have utility in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); incorporated by reference herein in its entirety.

[0244] As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalent and non-covalent conjugations) to polypeptides or other compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387; the disclosures of which are incorporated herein by reference in their entireties.

[0245] The antibodies of the invention include derivatives that are modified, i.e., by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

[0246] The antibodies of the present invention may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of- interest can be

produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: Monoclonal Antibodies and T-Cell Hybridomas 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

hybridoma technology are routine and well known in the art and are discussed in detail in the Examples. In a non-limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention.

Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

[0249] Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

[0250] Another well known method for producing both polyclonal and monoclonal human B cell lines is transformation using Epstein Barr Virus (EBV). Protocols for generating EBV-transformed B cell lines are commonly known in the art, such as, for example, the protocol outlined in Chapter 7.22 of Current Protocols in Immunology, Coligan et al., Eds., 1994, John Wiley & Sons, NY, which is hereby incorporated in its entirety by reference herein. The source of B cells for transformation is commonly human peripheral blood, but B cells for transformation may also be derived from other sources including, but not limited to, lymph nodes, tonsil, spleen, tumor tissue, and infected tissues. Tissues are generally made into single cell suspensions prior to EBV transformation. Additionally, steps may be taken to either physically remove or inactivate T cells (e.g., by treatment with cyclosporin A) in B cell-containing samples, because T cells from individuals seropositive for anti-EBV antibodies can suppress B cell immortalization by EBV.

In general, the sample containing human B cells is innoculated with EBV, and cultured for 3-4 weeks. A typical source of EBV is the culture supernatant of the B95-8 cell line (ATCC #VR-1492). Physical signs of EBV transformation can generally be seen towards the end of the 3-4 week culture period. By phase-contrast microscopy, transformed cells may appear large, clear, hairy and tend to aggregate in tight clusters of cells. Initially, EBV lines are generally polyclonal. However, over prolonged periods of cell cultures, EBV lines may become monoclonal or polyclonal as a result of the selective outgrowth of particular B cell clones. Alternatively, polyclonal EBV transformed lines may be subcloned (e.g., by limiting dilution culture) or fused with a suitable fusion partner and plated at limiting dilution to obtain

monoclonal B cell lines. Suitable fusion partners for EBV transformed cell lines include mouse myeloma cell lines (e.g., SP2/0, X63-Ag8.653), heteromyeloma cell lines (human x mouse; e.g, SPAM-8, SBC-H20, and CB-F7), and human cell lines (e.g., GM 1500, SKO-007, RPMI 8226, and KR-4). Thus, the present invention also provides a method of generating polyclonal or monoclonal human antibodies against polypeptides of the invention or fragments thereof, comprising EBV-transformation of human B cells.

[0252] Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')2 fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). F(ab')2 fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain. For example, the antibodies of the present invention can also be generated using various phage display methods known in the art and as discussed in detail in the Examples (e.g., Example 10). In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire or combinatorial antibody library (e.g., human or murine). expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., J. Immunol. Methods 182:41-50 (1995); Ames et al., J. Immunol. Methods 184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753;

5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

[0253] As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')2 fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

Examples of techniques which can be used to produce single-chain Fvs and [0254]antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999 (1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol. Methods 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the nonhuman species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve. antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework

residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

[0255] Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

Human antibodies can also be produced using transgenic mice which are [0256] incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against

the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, Int. Rev. Immunol. 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; 5,939,598; 6,075,181 and 6,114,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

[0257] Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., Bio/technology 12:899-903 (1988)).

[0258] Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotype antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, FASEB J. 7(5):437-444; (1989) and Nissinoff, J. Immunol. 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand/receptor. For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby block its biological activity.

Alternatively, antibodies which bind to and enhance polypeptide multimerization and/or binding, and/or receptor/ligand multimerization, binding and/or signaling can be used to generate anti-idiotypes that function as agonists of a polypeptide of the invention and/or its ligand/receptor. Such agonistic anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens as agonists of the polypeptides of the invention or its ligand(s)/receptor(s). For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby promote or enhance its biological activity.

Intrabodies of the invention can be produced using methods known in the art, such as those disclosed and reviewed in Chen et al., Hum. Gene Ther. 5:595-601 (1994); Marasco, W.A., Gene Ther. 4:11-15 (1997); Rondon and Marasco, Annu. Rev. Microbiol. 51:257-283 (1997); Proba et al., J. Mol. Biol. 275:245-253 (1998); Cohen et al., Oncogene 17:2445-2456 (1998); Ohage and Steipe, J. Mol. Biol. 291:1119-1128 (1999); Ohage et al., J. Mol. Biol. 291:1129-1134 (1999); Wirtz and Steipe, Protein Sci. 8:2245-2250 (1999); Zhu et al., J. Immunol. Methods 231:207-222 (1999); and references cited therein.

# Polynucleotides Encoding Antibodies

[0260] The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or alternatively, under lower stringency hybridization conditions, e.g., as defined *supra*, to polynucleotides that encode an antibody, preferably, that specifically binds to a polypeptide of the invention, preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y, to a polypeptide encoded by a portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or to a polypeptide encoded by the cDNA contained in Clone ID NO:Z.

[0261] The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., BioTechniques 17:242 (1994)), which, briefly, involves the synthesis

of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

[0263] Once the nucleotide sequence and corresponding amino acid sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel et al., eds., 1998, Current Protocols in Molecular Biology, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

[0264] In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well know in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a non-human

antibody, as described *supra*. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed *supra*, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

[0265] In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described *supra*, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423- 42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in *E. coli* may also be used (Skerra et al., Science 242:1038-1041 (1988)).

[0267] The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques. Methods of producing antibodies include, but are not limited to, hybridoma technology, EBV transformation, and other methods discussed herein as well as through the use recombinant DNA technology, as discussed below.

[0268] Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

[0269] The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light

chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

[0270] A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention in situ. These include but are not limited to microorganisms such as bacteria (e.g., E. coli, B. subtilis) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., Saccharomyces, Pichia) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as Escherichia coli, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., Gene 45:101 (1986); Cockett et al., Bio/Technology 8:2 (1990)).

[0271] In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule

being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the E. coli expression vector pUR278 (Ruther et al., EMBO J. 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, Nucleic Acids Res. 13:3101-3109 (1985); Van Heeke & Schuster, J. Biol. Chem. 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

[0272] In an insect system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in Spodoptera frugiperda cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

[0273] In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non- essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to

ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

[0274] In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the posttranslational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

[0275] For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule.

Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

[0276] A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed in tk-, hgprt- or aprt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 Clinical Pharmacy 12:488-505; Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); TIB TECH 11(5):155-215 (1993)); and hygro, which confers resistance to hygromycin (Santerre et al., Gene 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), Current Protocols in Human Genetics, John Wiley & Sons, NY (1994); Colberre-Garapin et al., J. Mol. Biol. 150:1 (1981), which are incorporated by reference herein in their entireties.

[0277] The expression levels of an antibody molecule can be increased by vector amplification (for a review, see Bebbington and Hentschel, The use of vectors based on gene amplification for the expression of cloned genes in mammalian cells in DNA cloning, Vol.3. (Academic Press, New York, 1987)). When a marker in the vector system expressing antibody is amplifiable, increase in the level of inhibitor present in culture of host cell will increase the number of copies of the marker gene. Since the amplified region is associated with the antibody gene, production of the antibody will also increase (Crouse et al., Mol. Cell. Biol. 3:257 (1983)).

Vectors which use glutamine synthase (GS) or DHFR as the selectable [0278] markers can be amplified in the presence of the drugs methionine sulphoximine or methotrexate, respectively. An advantage of glutamine synthase based vectors are the availabilty of cell lines (e.g., the murine myeloma cell line, NS0) which are glutamine synthase negative. Glutamine synthase expression systems can also function in glutamine synthase expressing cells (e.g., Chinese Hamster Ovary (CHO) cells) by providing additional inhibitor to prevent the functioning of the endogenous gene. A glutamine synthase expression system and components thereof are detailed in PCT publications: WO87/04462; WO86/05807; WO89/01036; WO89/10404; and WO91/06657 which are incorporated in their entireties by reference herein. Additionally, glutamine synthase expression vectors that may be used according to the present invention are commercially available from suplliers, including, for example Lonza Biologics, Inc. (Portsmouth, NH). Expression and production of monoclonal antibodies using a GS expression system in murine myeloma cells is described in Bebbington et al., Bio/technology 10:169(1992) and in Biblia and Robinson Biotechnol. Prog. 11:1 (1995) which are incorporated in their entirities by reference herein.

[0279] The host cell may be co-transfected with two expression vectors of the invention, the first vector encoding a heavy chain derived polypeptide and the second vector encoding a light chain derived polypeptide. The two vectors may contain identical selectable markers which enable equal expression of heavy and light chain polypeptides. Alternatively, a single vector may be used which encodes, and is capable of expressing, both heavy and light chain polypeptides. In such situations, the light chain should be placed before the heavy chain to avoid an excess of toxic free heavy chain (Proudfoot, Nature 322:52 (1986); Kohler, Proc. Natl. Acad. Sci. USA 77:2197 (1980)). The coding sequences for the heavy and light chains may comprise cDNA or genomic DNA.

[0280] Once an antibody molecule of the invention has been produced by an animal, chemically synthesized, or recombinantly expressed, it may be purified by any method known in the art for purification of an immunoglobulin molecule, for example, by chromatography (e.g., ion exchange, affinity, particularly by affinity for the specific antigen after Protein A, and sizing column chromatography), centrifugation,

differential solubility, or by any other standard technique for the purification of proteins. In addition, the antibodies of the present invention or fragments thereof can be fused to heterologous polypeptide sequences described herein or otherwise known in the art, to facilitate purification.

The present invention encompasses antibodies recombinantly fused or [0281] chemically conjugated (including both covalently and non-covalently conjugations) to a polypeptide (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention to generate fusion proteins. The fusion does not necessarily need to be direct, but may occur through linker sequences. The antibodies may be specific for antigens other than polypeptides (or portion thereof, preferably at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 amino acids of the polypeptide) of the present invention. For example, antibodies may be used to target the polypeptides of the present invention to particular cell types, either in vitro or in vivo, by fusing or conjugating the polypeptides of the present invention to antibodies specific for particular cell surface receptors. Antibodies fused or conjugated to the polypeptides of the present invention may also be used in in vitro immunoassays and purification methods using methods known in the art. See e.g., Harbor et al., supra, and PCT publication WO 93/21232; EP 439,095; Naramura et al., Immunol. Lett. 39:91-99 (1994); U.S. Patent 5,474,981; Gillies et al., PNAS 89:1428-1432 (1992); Fell et al., J. Immunol. 146:2446-2452 (1991), which are incorporated by reference in their entireties.

[0282] The present invention further includes compositions comprising the polypeptides of the present invention fused or conjugated to antibody domains other than the variable regions. For example, the polypeptides of the present invention may be fused or conjugated to an antibody Fc region, or portion thereof. The antibody portion fused to a polypeptide of the present invention may comprise the constant region, hinge region, CH1 domain, CH2 domain, and CH3 domain or any combination of whole domains or portions thereof. The polypeptides may also be fused or conjugated to the above antibody portions to form multimers. For example, Fc portions fused to the polypeptides of the present invention can form dimers through disulfide bonding between the Fc portions. Higher multimeric forms can be made by fusing the polypeptides to portions of IgA and IgM. Methods for fusing or

conjugating the polypeptides of the present invention to antibody portions are known in the art. See, e.g., U.S. Patent Nos. 5,336,603; 5,622,929; 5,359,046; 5,349,053; 5,447,851; 5,112,946; EP 307,434; EP 367,166; PCT publications WO 96/04388; WO 91/06570; Ashkenazi et al., Proc. Natl. Acad. Sci. USA 88:10535-10539 (1991); Zheng et al., J. Immunol. 154:5590-5600 (1995); and Vil et al., Proc. Natl. Acad. Sci. USA 89:11337- 11341 (1992) (said references incorporated by reference in their entireties).

[0283] As discussed, supra, the polypeptides corresponding to a polypeptide, polypeptide fragment, or a variant of SEQ ID NO:Y may be fused or conjugated to the above antibody portions to increase the in vivo half life of the polypeptides or for use in immunoassays using methods known in the art. Further, the polypeptides corresponding to SEQ ID NO:Y may be fused or conjugated to the above antibody portions to facilitate purification. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See EP 394,827; Traunecker et al., Nature 331:84-86 (1988). The polypeptides of the present invention fused or conjugated to an antibody having disulfide- linked dimeric structures (due to the IgG) may also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. See, for example, Fountoulakis et al., J. Biochem. 270:3958-3964 (1995). In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. See, for example, EP A 232,262. Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, Bennett et al., J. Molecular Recognition 8:52-58 (1995); Johanson et al., J. Biol. Chem. 270:9459-9471 (1995)).

[0284] Moreover, the antibodies or fragments thereof of the present invention can be fused to marker sequences, such as a peptide to facilitate purification. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the

tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexahistidine provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the "HA" tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)) and the "flag" tag.

The present invention further encompasses antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent. The antibodies can be used diagnostically to, for example, monitor the development or progression of a tumor as part of a clinical testing procedure to, e.g., determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, radioactive materials, positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions. The detectable substance may be coupled or conjugated either directly to the antibody (or fragment thereof) or indirectly, through an intermediate (such as, for example, a linker known in the art) using techniques known in the art. See, for example, U.S. Patent No. 4,741,900 for metal ions which can be conjugated to antibodies for use as diagnostics according to the present invention.

therapeutic moiety such as a cytotoxin, e.g., a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, 213Bi. A cytotoxin or cytotoxic agent includes any agent that is detrimental to cells. Examples include paclitaxol, cytochalasin B, gramicidin D, ethidium bromide, emetine, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicin, doxorubicin, daunorubicin, dihydroxy anthracin dione, mitoxantrone, mithramycin, actinomycin D, 1-dehydrotestosterone, glucocorticoids, procaine, tetracaine, lidocaine, propranolol, and puromycin and analogs or homologs thereof. Therapeutic agents include, but are not limited to, antimetabolites (e.g., methotrexate, 6-mercaptopurine, 6-thioguanine, cytarabine, 5-fluorouracil decarbazine), alkylating

agents (e.g., mechlorethamine, thioepa chlorambucil, melphalan, carmustine (BSNU) and lomustine (CCNU), cyclothosphamide, busulfan, dibromomannitol, streptozotocin, mitomycin C, and cis- dichlorodiamine platinum (II) (DDP) cisplatin), anthracyclines (e.g., daunorubicin (formerly daunomycin) and doxorubicin), antibiotics (e.g., dactinomycin (formerly actinomycin), bleomycin, mithramycin, and anthramycin (AMC)), and anti-mitotic agents (e.g., vincristine and vinblastine).

[0287] The conjugates of the invention can be used for modifying a given biological response, the therapeutic agent or drug moiety is not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, or diphtheria toxin; a protein such as tumor necrosis factor, a-interferon, ß-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, e.g., TNF-alpha, TNF-beta, AIM I (See, International Publication No. WO 97/33899), AIM II (See, International Publication No. WO 97/34911), Fas Ligand (Takahashi et al., Int. Immunol., 6:1567-1574 (1994)), VEGI (See, International Publication No. WO 99/23105), a thrombotic agent or an anti- angiogenic agent, e.g., angiostatin or endostatin; or, biological response modifiers such as, for example, lymphokines, interleukin-1 ("IL-1"), interleukin-2 ("IL-2"), interleukin-6 ("IL-6"), granulocyte macrophage colony stimulating factor ("GM-CSF"), granulocyte colony stimulating factor ("G-CSF"), or other growth factors.

[0288] Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

known. See, for example., Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal

Antibodies '84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", Immunol. Rev. 62:119-58 (1982).

[0290] Alternatively, an antibody can be conjugated to a second antibody to form an antibody heteroconjugate as described by Segal in U.S. Patent No. 4,676,980, which is incorporated herein by reference in its entirety.

[0291] An antibody, with or without a therapeutic moiety conjugated to it, administered alone or in combination with cytotoxic factor(s) and/or cytokine(s) can be used as a therapeutic.

# Immunophenotyping

[0292] The antibodies of the invention may be utilized for immunophenotyping of cell lines and biological samples. Translation products of the genes of the present invention may be useful as cell specific markers, or more specifically as cellular markers that are differentially expressed at various stages of differentiation and/or maturation of particular cell types. Monoclonal antibodies directed against a specific epitope, or combination of epitopes, will allow for the screening of cellular populations expressing the marker. Various techniques can be utilized using monoclonal antibodies to screen for cellular populations expressing the marker(s), and include magnetic separation using antibody-coated magnetic beads, "panning" with antibody attached to a solid matrix (i.e., plate), and flow cytometry (See, e.g., U.S. Patent 5,985,660; and Morrison et al., Cell, 96:737-49 (1999)).

[0293] These techniques allow for the screening of particular populations of cells, such as might be found with hematological malignancies (i.e. minimal residual disease (MRD) in acute leukemic patients) and "non-self" cells in transplantations to prevent Graft-versus-Host Disease (GVHD). Alternatively, these techniques allow for the screening of hematopoietic stem and progenitor cells capable of undergoing proliferation and/or differentiation, as might be found in human umbilical cord blood.

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nylon, blocking the membrane in blocking solution (e.g., PBS with 3% BSA or non-fat milk), washing the membrane in washing buffer (e.g., PBS-Tween 20), blocking the membrane with primary antibody (the antibody of interest) diluted in blocking buffer, washing the membrane in washing buffer, blocking the membrane with a secondary antibody (which recognizes the primary antibody, e.g., an anti-human antibody) conjugated to an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) or radioactive molecule (e.g., 32P or 125I) diluted in blocking buffer, washing the membrane in wash buffer, and detecting the presence of the antigen. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected and to reduce the background noise. For further discussion regarding western blot protocols see, e.g., Ausubel et al., eds., (1994), Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 10.8.1.

[0297] ELISAs comprise preparing antigen, coating the well of a 96 well microtiter plate with the antigen, adding the antibody of interest conjugated to a detectable compound such as an enzymatic substrate (e.g., horseradish peroxidase or alkaline phosphatase) to the well and incubating for a period of time, and detecting the presence of the antigen. In ELISAs the antibody of interest does not have to be conjugated to a detectable compound; instead, a second antibody (which recognizes the antibody of interest) conjugated to a detectable compound may be added to the well. Further, instead of coating the well with the antigen, the antibody may be coated to the well. In this case, a second antibody conjugated to a detectable compound may be added following the addition of the antigen of interest to the coated well. One of skill in the art would be knowledgeable as to the parameters that can be modified to increase the signal detected as well as other variations of ELISAs known in the art. For further discussion regarding ELISAs see, e.g., Ausubel et al., eds., (1994), Current Protocols in Molecular Biology, Vol. 1, John Wiley & Sons, Inc., New York, section 11.2.1.

[0298] The binding affinity of an antibody to an antigen and the off-rate of an antibody-antigen interaction can be determined by competitive binding assays. One example of a competitive binding assay is a radioimmunoassay comprising the incubation of labeled antigen (e.g., 3H or 125I) with the antibody of interest in the

presence of increasing amounts of unlabeled antigen, and the detection of the antibody bound to the labeled antigen. The affinity of the antibody of interest for a particular antigen and the binding off-rates can be determined from the data by scatchard plot analysis. Competition with a second antibody can also be determined using radioimmunoassays. In this case, the antigen is incubated with antibody of interest conjugated to a labeled compound (e.g., 3H or 125I) in the presence of increasing amounts of an unlabeled second antibody.

[0299] Antibodies of the invention may be characterized using immunocytochemisty methods on cells (e.g., mammalian cells, such as CHO cells) transfected with a vector enabling the expression of a reproductive system antigen or with vector alone using techniques commonly known in the art. Antibodies that bind reproductive system antigen transfected cells, but not vector-only transfected cells, are reproductive system antigen specific.

# Therapeutic Uses

The present invention is further directed to antibody-based therapies which [0300] involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the disclosed diseases, disorders, or conditions. Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to treat, inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions described herein. The treatment and/or prevention of diseases, disorders, or conditions associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

[0301] In a specific and preferred embodiment, the present invention is directed to antibody-based therapies which involve administering antibodies of the invention to an animal, preferably a mammal, and most preferably a human, patient for treating one or more of the diseases, disorders, or conditions of the reproductive system, including, but not limited to, injuries and trauma, infections, neoplastic disorders, congenital defects, and diseases or disorders which result in infertility, complications with pregnancy, labor, or parturition, postpartum difficulties, and as listed below in the section entitled "Reproductive System Disorders". Therapeutic compounds of the invention include, but are not limited to, antibodies of the invention (e.g., antibodies directed to the full length protein expressed on the cell surface of a mammalian cell; antibodies directed to an epitope of a reproductive system associated polypeptide of the invention (such as, a linear epitope (shown in Table 1A, column 6) or a conformational epitope), including fragments, analogs and derivatives thereof as described herein) and nucleic acids encoding antibodies of the invention (including fragments, analogs and derivatives thereof and anti-idiotypic antibodies as described herein). The antibodies of the invention can be used to treat, inhibit or prevent diseases, disorders or conditions associated with aberrant expression and/or activity of a polypeptide of the invention, including, but not limited to, any one or more of the diseases, disorders, or conditions of the reproductive system described herein. The treatment and/or prevention of diseases, disorders, or conditions of the reproductive system associated with aberrant expression and/or activity of a polypeptide of the invention includes, but is not limited to, alleviating symptoms associated with those diseases, disorders or conditions. Antibodies of the invention may be provided in pharmaceutically acceptable compositions as known in the art or as described herein.

[0302] A summary of the ways in which the antibodies of the present invention may be used therapeutically includes binding polynucleotides or polypeptides of the present invention locally or systemically in the body or by direct cytotoxicity of the antibody, e.g. as mediated by complement (CDC) or by effector cells (ADCC). Some of these approaches are described in more detail below. Armed with the teachings provided herein, one of ordinary skill in the art will know how to use the antibodies of the present invention for diagnostic, monitoring or therapeutic purposes without undue experimentation.

[0303] The antibodies of this invention may be advantageously utilized in combination with other monoclonal or chimeric antibodies, or with lymphokines or hematopoietic growth factors (such as, e.g., IL-2, IL-3 and IL-7), for example, which serve to increase the number or activity of effector cells which interact with the antibodies.

[0304] The antibodies of the invention may be administered alone or in combination with other types of treatments (e.g., radiation therapy, chemotherapy, hormonal therapy, immunotherapy and anti-tumor agents). Generally, administration of products of a species origin or species reactivity (in the case of antibodies) that is the same species as that of the patient is preferred. Thus, in a preferred embodiment, human antibodies, fragments derivatives, analogs, or nucleic acids, are administered to a human patient for therapy or prophylaxis.

[0305] It is preferred to use high affinity and/or potent *in vivo* inhibiting and/or neutralizing antibodies against polypeptides or polynucleotides of the present invention, fragments or regions thereof, for both immunoassays directed to and therapy of disorders related to polynucleotides or polypeptides, including fragments thereof, of the present invention. Such antibodies, fragments, or regions, will preferably have an affinity for polynucleotides or polypeptides of the invention, including fragments thereof. Preferred binding affinities include those with a dissociation constant or Kd less than 5 X 10<sup>-2</sup> M, 10<sup>-2</sup> M, 5 X 10<sup>-3</sup> M, 10<sup>-3</sup> M, 5 X 10<sup>-8</sup> M, 10<sup>-4</sup> M, 5 X 10<sup>-5</sup> M, 10<sup>-5</sup> M, 5 X 10<sup>-6</sup> M, 10<sup>-6</sup> M, 5 X 10<sup>-7</sup> M, 10<sup>-7</sup> M, 5 X 10<sup>-8</sup> M, 10<sup>-8</sup> M, 5 X 10<sup>-9</sup> M, 10<sup>-9</sup> M, 5 X 10<sup>-10</sup> M, 10<sup>-10</sup> M, 5 X 10<sup>-11</sup> M, 10<sup>-11</sup> M, 5 X 10<sup>-12</sup> M, 10<sup>-12</sup> M, 5 X 10<sup>-13</sup> M, 10<sup>-13</sup> M, 5 X 10<sup>-14</sup> M, 10<sup>-14</sup> M, 5 X 10<sup>-15</sup> M, and 10<sup>-15</sup> M.

### Gene Therapy

[0306] In a specific embodiment, nucleic acids comprising sequences encoding antibodies or functional derivatives thereof, are administered to treat, inhibit or prevent a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. Gene therapy refers to therapy performed by the administration to a subject of an expressed or expressible nucleic acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

[0307] Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

[0308] For general reviews of the methods of gene therapy, see Goldspiel et al., Clinical Pharmacy 12:488-505 (1993); Wu and Wu, Biotherapy 3:87-95 (1991); Tolstoshev, Ann. Rev. Pharmacol. Toxicol. 32:573-596 (1993); Mulligan, Science 260:926-932 (1993); and Morgan and Anderson, Ann. Rev. Biochem. 62:191-217 (1993); May, TIBTECH 11(5):155-215 (1993). Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), Current Protocols in Molecular Biology, John Wiley & Sons, NY (1993); and Kriegler, Gene Transfer and Expression, A Laboratory Manual, Stockton Press, NY (1990).

[0309] In a preferred embodiment, the compound comprises nucleic acid sequences encoding an antibody, said nucleic acid sequences being part of expression vectors that express the antibody or fragments or chimeric proteins or heavy or light chains thereof in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the antibody coding region, said promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment, nucleic acid molecules are used in which the antibody coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the antibody encoding nucleic acids (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989). In specific embodiments, the expressed antibody molecule is a single chain antibody; alternatively, the nucleic acid sequences include sequences encoding both the heavy and light chains, or fragments thereof, of the antibody.

[0310] Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid- carrying vectors, or indirect, in which case, cells are first transformed with the nucleic acids in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

[0311] In a specific embodiment, the nucleic acid sequences are directly administered in vivo, where it is expressed to produce the encoded product. This can

be accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Patent No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic acidligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted in vivo for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); Zijlstra et al., Nature 342:435-438 (1989)).

[0312] In a specific embodiment, viral vectors that contains nucleic acid sequences encoding an antibody of the invention are used. For example, a retroviral vector can be used (see Miller et al., Meth. Enzymol. 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., Biotherapy 6:291-302 (1994), which describes the use of a retroviral vector to deliver the mdr1 gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., J. Clin. Invest. 93:644-651 (1994); Kiem et al., Blood 83:1467-1473 (1994); Salmons and Gunzberg, Human

Gene Therapy 4:129-141 (1993); and Grossman and Wilson, Curr. Opin. in Genetics and Devel. 3:110-114 (1993).

- Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, Current Opinion in Genetics and Development 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., Human Gene Therapy 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., Science 252:431-434 (1991); Rosenfeld et al., Cell 68:143- 155 (1992); Mastrangeli et al., J. Clin. Invest. 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., Gene Therapy 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.
- [0314] Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., Proc. Soc. Exp. Biol. Med. 204:289-300 (1993); U.S. Patent No. 5,436,146).
- [0315] Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.
- [0316] In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see,

e.g., Loeffler and Behr, Meth. Enzymol. 217:599-618 (1993); Cohen et al., Meth. Enzymol. 217:618-644 (1993); Cline, Pharmac. Ther. 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

- [0317] The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.
- [0318] Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as T lymphocytes, B lymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.
- [0319] In a preferred embodiment, the cell used for gene therapy is autologous to the patient.
- In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding an antibody are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, Cell 71:973-985 (1992); Rheinwald, Meth. Cell Bio. 21A:229 (1980); and Pittelkow and Scott, Mayo Clinic Proc. 61:771 (1986)).
- [0321] In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region,

such that expression of the nucleic acid is controllable by the presence or absence of an appropriate inducer of transcription.

## Demonstration of Therapeutic or Prophylactic Activity

preferably tested *in vitro*, and then *in vivo* for the desired therapeutic or prophylactic activity, prior to use in humans. For example, *in vitro* assays to demonstrate the therapeutic or prophylactic utility of a compound or pharmaceutical composition include, the effect of a compound on a cell line or a patient tissue sample. The effect of the compound or composition on the cell line and/or tissue sample can be determined utilizing techniques known to those of skill in the art including, but not limited to, rosette formation assays and cell lysis assays. In accordance with the invention, *in vitro* assays which can be used to determine whether administration of a specific compound is indicated, include *in vitro* cell culture assays in which a patient tissue sample is grown in culture, and exposed to or otherwise administered a compound, and the effect of such compound upon the tissue sample is observed.

# Therapeutic/Prophylactic Administration and Composition

- [0323] The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical composition of the invention, preferably a polypeptide or antibody of the invention. In a preferred embodiment, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce undesired side-effects). The subject is preferably an animal, including but not limited to animals such as cows, pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.
- [0324] Formulations and methods of administration that can be employed when the compound comprises a nucleic acid or an immunoglobulin are described above; additional appropriate formulations and routes of administration can be selected from among those described herein below.
- [0325] Various delivery systems are known and can be used to administer a compound of the invention, e.g., encapsulation in liposomes, microparticles,

microcapsules, recombinant cells capable of expressing the compound, receptormediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds or compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

- [0326] In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when administering a protein, including an antibody, of the invention, care must be taken to use materials to which the protein does not absorb.
- [0327] In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, Science 249:1527-1533 (1990); Treat et al., in Liposomes in the Therapy of Infectious Disease and Cancer, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, ibid., pp. 317-327; see generally ibid.)
- [0328] In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, supra; Sefton, CRC Crit. Ref. Biomed. Eng. 14:201 (1987); Buchwald et al., Surgery

88:507 (1980); Saudek et al., N. Engl. J. Med. 321:574 (1989)). In another embodiment, polymeric materials can be used (see Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Florida (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., Macromol. Sci. Rev. Macromol. Chem. 23:61 (1983); see also Levy et al., Science 228:190 (1985); During et al., Ann. Neurol. 25:351 (1989); Howard et al., J.Neurosurg. 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, e.g., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, *supra*, vol. 2, pp. 115-138 (1984)).

- [0329] Other controlled release systems are discussed in the review by Langer (Science 249:1527-1533 (1990)).
- In a specific embodiment where the compound of the invention is a nucleic acid encoding a protein, the nucleic acid can be administered *in vivo* to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (see e.g., Joliot et al., Proc. Natl. Acad. Sci. USA 88:1864-1868 (1991)), etc. Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.
- [0331] The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and

oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E.W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

[0332] In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition

is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

[0333] The compounds of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

[0334] The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

[0335] For antibodies, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human antibodies have a longer half-life within the human body than antibodies from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human antibodies and less frequent administration is often possible. Further, the dosage and frequency of administration of antibodies of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the antibodies by modifications such as, for example, lipidation.

[0336] The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture,

use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

## Diagnosis and Imaging

Labeled antibodies, and derivatives and analogs thereof, which specifically bind to a polypeptide of interest can be used for diagnostic purposes to detect, diagnose, or monitor diseases, disorders, and/or conditions associated with the aberrant expression and/or activity of a polypeptide of the invention. The invention provides for the detection of aberrant expression of a polypeptide of interest, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of aberrant expression.

The invention provides a diagnostic assay for diagnosing a reproductive system disorder, comprising (a) assaying the expression of the polypeptide of interest in cells or body fluid of an individual using one or more antibodies specific to the polypeptide interest and (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a particular disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

[0339] Antibodies of the invention can be used to assay protein levels in a biological sample using classical immunohistological methods known to those of skill in the art (e.g., see Jalkanen et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen et al., J. Cell . Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked

immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and technetium (99Tc); luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

[0340] One facet of the invention is the detection and diagnosis of a disease or disorder associated with aberrant expression of a polypeptide of interest in an animal, preferably a mammal and most preferably a human. A preferred embodiment of the invention is the detection and diagnosis of a disease or disorder of the reproductive system associated with aberrant expression of a reproductive system antigen in an animal, preferably a mammal and most preferably a human. In one embodiment, diagnosis comprises: a) administering (for example, parenterally, subcutaneously, or intraperitoneally) to a subject an effective amount of a labeled molecule which specifically binds to the polypeptide of interest; b) waiting for a time interval following the administering for permitting the labeled molecule to preferentially concentrate at sites in the subject where the polypeptide is expressed (and for unbound labeled molecule to be cleared to background level); c) determining background level; and d) detecting the labeled molecule in the subject, such that detection of labeled molecule above the background level indicates that the subject has a particular disease or disorder associated with aberrant expression of the polypeptide of interest. Background level can be determined by various methods including, comparing the amount of labeled molecule detected to a standard value previously determined for a particular system.

It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. *In vivo* tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The

Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

- [0342] Depending on several variables, including the type of label used and the mode of administration, the time interval following the administration for permitting the labeled molecule to preferentially concentrate at sites in the subject and for unbound labeled molecule to be cleared to background level is 6 to 48 hours or 6 to 24 hours or 6 to 12 hours. In another embodiment the time interval following administration is 5 to 20 days or 5 to 10 days.
- [0343] In an embodiment, monitoring of the disease or disorder is carried out by repeating the method for diagnosing the disease or disorder, for example, one month after initial diagnosis, six months after initial diagnosis, one year after initial diagnosis, etc.
- [0344] Presence of the labeled molecule can be detected in the patient using methods known in the art for *in vivo* scanning. These methods depend upon the type of label used. Skilled artisans will be able to determine the appropriate method for detecting a particular label. Methods and devices that may be used in the diagnostic methods of the invention include, but are not limited to, computed tomography (CT), whole body scan such as position emission tomography (PET), magnetic resonance imaging (MRI), and sonography.
- [0345] In a specific embodiment, the molecule is labeled with a radioisotope and is detected in the patient using a radiation responsive surgical instrument (Thurston et al., U.S. Patent No. 5,441,050). In another embodiment, the molecule is labeled with a fluorescent compound and is detected in the patient using a fluorescence responsive scanning instrument. In another embodiment, the molecule is labeled with a positron emitting metal and is detected in the patent using positron emission-tomography. In yet another embodiment, the molecule is labeled with a paramagnetic label and is detected in a patient using magnetic resonance imaging (MRI).

Kits

[0346] The present invention provides kits that can be used in the above methods. In one embodiment, a kit comprises an antibody of the invention, preferably a purified antibody, in one or more containers. In a specific embodiment, the kits of the present

invention contain a substantially isolated polypeptide comprising an epitope which is specifically immunoreactive with an antibody included in the kit. Preferably, the kits of the present invention further comprise a control antibody which does not react with the polypeptide of interest. In another specific embodiment, the kits of the present invention contain a means for detecting the binding of an antibody to a polypeptide of interest (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent compound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate).

[0347] In another specific embodiment of the present invention, the kit is a diagnostic kit for use in screening serum containing antibodies specific against proliferative and/or cancerous polynucleotides and polypeptides. Such a kit may include a control antibody that does not react with the polypeptide of interest. Such a kit may include a substantially isolated polypeptide antigen comprising an epitope which is specifically immunoreactive with at least one anti-polypeptide antigen antibody. Further, such a kit includes means for detecting the binding of said antibody to the antigen (e.g., the antibody may be conjugated to a fluorescent compound such as fluorescein or rhodamine which can be detected by flow cytometry). In specific embodiments, the kit may include a recombinantly produced or chemically synthesized polypeptide antigen. The polypeptide antigen of the kit may also be attached to a solid support.

[0348] In a more specific embodiment the detecting means of the above-described kit includes a solid support to which said polypeptide antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the polypeptide antigen can be detected by binding of the said reporter-labeled antibody.

[0349] In an additional embodiment, the invention includes a diagnostic kit for use in screening serum containing antigens of the polypeptide of the invention. The diagnostic kit includes a substantially isolated antibody specifically immunoreactive with polypeptide or polynucleotide antigens, and means for detecting the binding of the polynucleotide or polypeptide antigen to the antibody. In one embodiment, the antibody is attached to a solid support. In a specific embodiment, the antibody may be

a monoclonal antibody. The detecting means of the kit may include a second, labeled monoclonal antibody. Alternatively, or in addition, the detecting means may include a labeled, competing antigen.

[0350] In one diagnostic configuration, test serum is reacted with a solid phase reagent having a surface-bound antigen obtained by the methods of the present invention. After binding with specific antigen antibody to the reagent and removing unbound serum components by washing, the reagent is reacted with reporter-labeled anti-human antibody to bind reporter to the reagent in proportion to the amount of bound anti-antigen antibody on the solid support. The reagent is again washed to remove unbound labeled antibody, and the amount of reporter associated with the reagent is determined. Typically, the reporter is an enzyme which is detected by incubating the solid phase in the presence of a suitable fluorometric, luminescent or colorimetric substrate (Sigma, St. Louis, MO).

[0351] The solid surface reagent in the above assay is prepared by known techniques for attaching protein material to solid support material, such as polymeric beads, dip sticks, 96-well plate or filter material. These attachment methods generally include non-specific adsorption of the protein to the support or covalent attachment of the protein, typically through a free amine group, to a chemically reactive group on the solid support, such as an activated carboxyl, hydroxyl, or aldehyde group. Alternatively, streptavidin coated plates can be used in conjunction with biotinylated antigen(s).

[0352] Thus, the invention provides an assay system or kit for carrying out this diagnostic method. The kit generally includes a support with surface-bound recombinant antigens, and a reporter-labeled anti-human antibody for detecting surface-bound anti-antigen antibody.

### Uses of the Polynucleotides

[0353] Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

[0354] The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat polymorphisms), are presently available. Each sequence is specifically targeted to and can hybridize with a particular location on an individual human chromosome, thus each polynucleotide of the present invention can routinely be used as a chromosome marker using techniques known in the art. Table 1A, column 8 provides the chromosome location of some of the polynucleotides of the invention.

[0355] Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably at least 15 bp (e.g., 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can optionally be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to SEQ ID NO:X will yield an amplified fragment.

[0356] Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, preselection by hybridization to construct chromosome specific-cDNA libraries, and computer mapping techniques (See, e.g., Shuler, Trends Biotechnol 16:456-459 (1998) which is hereby incorporated by reference in its entirety).

[0357] Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

[0358] For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes).

- [0359] Thus, the present invention also provides a method for chromosomal localization which involves (a) preparing PCR primers from the polynucleotide sequences in Table 1A and/or Table 2 and SEQ ID NO:X and (b) screening somatic cell hybrids containing individual chromosomes.
- [0360] The polynucleotides of the present invention would likewise be useful for radiation hybrid mapping, HAPPY mapping, and long range restriction mapping. For a review of these techniques and others known in the art, see, e.g. Dear, "Genome Mapping: A Practical Approach," IRL Press at Oxford University Press, London (1997); Aydin, J. Mol. Med. 77:691-694 (1999); Hacia et al., Mol. Psychiatry 3:483-492 (1998); Herrick et al., Chromosome Res. 7:409-423 (1999); Hamilton et al., Methods Cell Biol. 62:265-280 (2000); and/or Ott, J. Hered. 90:68-70 (1999), each of which is hereby incorporated by reference in its entirety.
- [0361] Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library).) Column 9 of Table 1A provides an OMIM reference identification number of diseases associated with the cytologic band disclosed in column 8 of Table 1A, as determined using techniques described herein and by reference to Table 5. Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.
- [0362] Thus, once coinheritance is established, differences in a polynucleotide of the invention and the corresponding gene between affected and unaffected individuals can be examined. First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates

that mutations may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

[0363] Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using the polynucleotides of the invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker. Diagnostic and prognostic methods, kits and reagents encompassed by the present invention are briefly described below and more thoroughly elsewhere herein (see e.g., the sections labeled "Antibodies", "Diagnostic Assays", and "Methods for Detecting Reproductive System Disease, Including Cancer").

[0364] Thus, the invention also provides a diagnostic method useful during diagnosis of a disorder, involving measuring the expression level of polynucleotides of the present invention in cells or body fluid from an individual and comparing the measured gene expression level with a standard level of polynucleotide expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a disorder. Additional non-limiting examples of diagnostic methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., Example 12).

[0365] In still another embodiment, the invention includes a kit for analyzing samples for the presence of proliferative and/or cancerous polynucleotides derived from a test subject, as further described herein. In a general embodiment, the kit includes at least one polynucleotide probe containing a nucleotide sequence that will specifically hybridize with a polynucleotide of the invention and a suitable container. In a specific embodiment, the kit includes two polynucleotide probes defining an internal region of the polynucleotide of the invention, where each probe has one strand containing a 31'mer-end internal to the region. In a further embodiment, the probes may be useful as primers for polymerase chain reaction amplification.

[0366] Where a diagnosis of a related disorder, including, for example, diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or

depressed polynucleotide of the invention expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

[0367] By "measuring the expression level of polynucleotides of the invention" is intended qualitatively or quantitatively measuring or estimating the level of the polypeptide of the invention or the level of the mRNA encoding the polypeptide of the invention in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the polypeptide level or mRNA level in a second biological sample). Preferably, the polypeptide level or mRNA level in the first biological sample is measured or estimated and compared to a standard polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the related disorder or being determined by averaging levels from a population of individuals not having a related disorder. As will be appreciated in the art, once a standard polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

[0368] By "biological sample" is intended any biological sample obtained from an individual, body fluid, cell line, tissue culture, or other source which contains polypeptide of the present invention or the corresponding mRNA. As indicated, biological samples include body fluids (such as semen, lymph, vaginal pool, sera, plasma, urine, synovial fluid and spinal fluid) which contain the polypeptide of the present invention, and tissue sources found to express the polypeptide of the present invention. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the biological sample is to include mRNA, a tissue biopsy is the preferred source.

[0369] The method(s) provided above may preferably be applied in a diagnostic method and/or kits in which polynucleotides and/or polypeptides of the invention are attached to a solid support. In one exemplary method, the support may be a "gene chip" or a "biological chip" as described in U.S. Patents 5,837,832, 5,874,219, and 5,856,174. Further, such a gene chip with polynucleotides of the invention attached may be used to identify polymorphisms between the isolated polynucleotide sequences of the invention, with polynucleotides isolated from a test subject. The knowledge of such polymorphisms (i.e., their location, as well as, their existence) would be

beneficial in identifying disease loci for many disorders, such as for example, in neural disorders, immune system disorders, muscular disorders, reproductive disorders, gastrointestinal disorders, pulmonary disorders, digestive disorders, cardiovascular disorders, renal disorders, proliferative disorders, and/or cancerous diseases and conditions. Such a method is described in U.S. Patents 5,858,659 and 5,856,104. The U.S. Patents referenced *supra* are hereby incorporated by reference in their entirety herein.

[0370] The present invention encompasses polynucleotides of the present invention that are chemically synthesized, or reproduced as peptide nucleic acids (PNA), or according to other methods known in the art. The use of PNAs would serve as the preferred form if the polynucleotides of the invention are incorporated onto a solid support, or gene chip. For the purposes of the present invention, a peptide nucleic acid (PNA) is a polyamide type of DNA analog and the monomeric units for adenine, guanine, thymine and cytosine are available commercially (Perceptive Biosystems). Certain components of DNA, such as phosphorus, phosphorus oxides, or deoxyribose derivatives, are not present in PNAs. As disclosed by Nielsen et al., Science 254:1497 (1991); and Egholm et al., Nature 365:666 (1993), PNAs bind specifically and tightly to complementary DNA strands and are not degraded by nucleases. In fact, PNA binds more strongly to DNA than DNA itself does. This is probably because there is no electrostatic repulsion between the two strands, and also the polyamide backbone is more flexible. Because of this, PNA/DNA duplexes bind under a wider range of stringency conditions than DNA/DNA duplexes, making it easier to perform multiplex hybridization. Smaller probes can be used than with DNA due to the strong binding. In addition, it is more likely that single base mismatches can be determined with PNA/DNA hybridization because a single mismatch in a PNA/DNA 15-mer lowers the melting point (T.sub.m) by 8°-20° C, vs. 4°-16° C for the DNA/DNA 15-mer duplex. Also, the absence of charge groups in PNA means that hybridization can be done at low ionic strengths and reduce possible interference by salt during the analysis.

[0371] The compounds of the present invention have uses which include, but are not limited to, detecting cancer in mammals. In particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: acute myelogenous leukemias including acute monocytic leukemia.

acute myeloblastic leukemia, acute promyelocytic leukemia, acute myelomonocytic leukemia, acute erythroleukemia, acute megakaryocytic leukemia, and acute undifferentiated leukemia, etc.; and chronic myelogenous leukemias including chronic myelomonocytic leukemia, chronic granulocytic leukemia, etc. Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

[0372] The compounds of the present invention have preferred uses which include, but are not limited to, detecting reproductive system cancers in mammals. particular the invention is useful during diagnosis of pathological cell proliferative neoplasias which include, but are not limited to: testicular cancers (including, for example, teratocarcinoma, embryonal cell carcinoma, yolk sac tumors, Leydig cell tumors, and as listed below in the section entitiled "Reproductive System Disorders"), prostate cancers (e.g., adenocarcinomas, transitional cell carcinomas, ductal carcinomas, squamous cell carcinomas, and as listed below in the section entitled "Reproductive System Disorders"), penile cancers (such as squamous cell carcinoma, verrucous carcinoma, penile urethral carcinoma, and as listed below in the section entitled "Reproductive System Disorders"), cancers of the vagina and vulva (including, for example, basal cell carcinoma, melanomas, cancer of Bartholin's gland, and as listed below in the section entitled "Reproductive System Disorders"), uterine cancers (such as adenocarcinomas, keiomyosarcomas, and as listed below in the section entitled "Reproductive System Disorders"), ovarian cancers (e.g., Sertoli-Leydig tumors, endometriod carcinoma of the ovary, ovarian papollary serous adenocarcinoma, ovarian Krukenberg tumors, and as listed below in the section entitled "Reproductive System Disorders"), and cancers of the cervix (including, for example, squamous metaplasia, columnar cell neoplasia, squamous cell carcinoma, and as listed below in the section entitled "Reproductive System Disorders"). Preferred mammals include monkeys, apes, cats, dogs, cows, pigs, horses, rabbits and humans. Particularly preferred are humans.

[0373] Pathological cell proliferative disorders are often associated with inappropriate activation of proto-oncogenes. (Gelmann, E. P. et al., "The Etiology of Acute Leukemia: Molecular Genetics and Viral Oncology," in Neoplastic Diseases of the Blood, Vol 1., Wiernik, P. H. et al. eds., 161-182 (1985)). Neoplasias are now

believed to result from the qualitative alteration of a normal cellular gene product, or from the quantitative modification of gene expression by insertion into the chromosome of a viral sequence, by chromosomal translocation of a gene to a more actively transcribed region, or by some other mechanism. (Gelmann et al., supra) It is likely that mutated or altered expression of specific genes is involved in the pathogenesis of some leukemias, among other tissues and cell types. (Gelmann et al., supra) Indeed, the human counterparts of the oncogenes involved in some animal neoplasias have been amplified or translocated in some cases of human leukemia and carcinoma. (Gelmann et al., supra)

[0374] For example, c-myc expression is highly amplified in the non-lymphocytic leukemia cell line HL-60. When HL-60 cells are chemically induced to stop proliferation, the level of c-myc is found to be downregulated. (International Publication Number WO 91/15580). However, it has been shown that exposure of HL-60 cells to a DNA construct that is complementary to the 5' end of c-myc or c-myb blocks translation of the corresponding mRNAs which downregulates expression of the c-myc or c-myb proteins and causes arrest of cell proliferation and differentiation of the treated cells. (International Publication Number WO 91/15580; Wickstrom et al., Proc. Natl. Acad. Sci. 85:1028 (1988); Anfossi et al., Proc. Natl. Acad. Sci. 86:3379 (1989)). However, the skilled artisan would appreciate the present invention's usefulness is not be limited to treatment, prevention, diagnosis and/or prognosis, of proliferative disorders of cells and tissues of hematopoietic origin, in light of the numerous cells and cell types of varying origins which are known to exhibit proliferative phenotypes. In preferred embodiments, the compounds and/or methods of the invention are used to treat, prevent, diagnose, and/or prognose, proliferative disorders of reproductive system cells and tissues.

[0375] In addition to the foregoing, a polynucleotide of the present invention can be used to control gene expression through triple helix formation or through antisense DNA or RNA. Antisense techniques are discussed, for example, in Okano, J. Neurochem. 56: 560 (1991); "Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988). Triple helix formation is discussed in, for instance Lee et al., Nucleic Acids Research 6: 3073 (1979); Cooney et al., Science 241: 456 (1988); and Dervan et al., Science 251: 1360 (1991). Both methods rely on

binding of the polynucleotide to a complementary DNA or RNA. For these techniques, preferred polynucleotides are usually oligonucleotides 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. The oligonucleotide described above can also be delivered to cells such that the antisense RNA or DNA may be expressed in vivo to inhibit production of polypeptide of the present invention antigens. Both techniques are effective in model systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease, and in particular, for the treatment of proliferative diseases and/or conditions. Non-limiting antisense and triple helix methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., the section labeled "Antisense and Ribozyme (Antagonists)").

One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell. Additional non-limiting examples of gene therapy methods encompassed by the present invention are more thoroughly described elsewhere herein (see, e.g., the sections labeled "Gene Therapy Methods" and Examples 16, 17 and 18).

[0377] The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for

identifying personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

[0378] The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

[0379] Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, synovial fluid, amniotic fluid, breast milk, lymph, pulmonary sputum or surfactant, urine, fecal matter, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

[0380] There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers prepared from the sequences of the present invention, specific to tissues, including but not limited to, those sequences referred to in Table 1A. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination. Additional non-limiting examples of such uses are further described herein.

[0381] Because reproductive system antigens are found expressed in reproductive system tissues, the polynucleotides of the present invention are also useful as hybridization probes for differential identification of the tissue(s) or cell type(s) present in a biological sample. Similarly, polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In a specific embodiment, the polynucleotides of the present invention are also useful as hybridization probes for differential identification of reproductive system tissue(s) or cell type(s) present in a biological sample. Similarly, polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of reproductive system tissue(s) (e.g., immunohistochemistry assays) or cell type(s) (e.g., immunocytochemistry assays). In addition, for a number of disorders of the above tissues or cells, significantly higher or lower levels of gene expression of the polynucleotides/polypeptides of the present invention may be detected in certain tissues (e.g., tissues expressing polypeptides and/or polynucleotides of the present invention, for example, normal reproductive system tissues or diseased reproductive system tissues, and/or those tissues/cells corresponding to the library source relating to a polynucleotide sequence of the invention as disclosed in column 7 of Table 1A, and/or cancerous and/or wounded tissues) or bodily fluids (e.g., semen, lymph, vaginal pool, serum, plasma, urine, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a "standard" gene expression level, i.e., the expression level in healthy tissue from an individual not having the disorder.

[0382] Thus, the invention provides a diagnostic method of a disorder, which involves: (a) assaying gene expression level in cells or body fluid of an individual; (b) comparing the gene expression level with a standard gene expression level, whereby an increase or decrease in the assayed gene expression level compared to the standard expression level is indicative of a disorder.

[0383] In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and

making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

#### Uses of the Polypeptides

[0384] Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

[0385] Polypeptides and antibodies directed to polypeptides of the present invention are useful to provide immunological probes for differential identification of the tissue(s) (e.g., immunohistochemistry assays such as, for example, ABC immunoperoxidase (Hsu et al., J. Histochem. Cytochem. 29:577-580 (1981)) or cell type(s) (e.g., immunocytochemistry assays).

polynucleotides can be used to assay levels of polypeptides encoded by polynucleotides of the invention in a biological sample using classical immunohistological methods known to those of skill in the art (see, e.g., Jalkanen, et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, et al., J. Cell. Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase; radioisotopes, such as iodine (131 I, 125 I, 123 I, 121 I), carbon (14C), sulfur (35S), tritium (3H), indium (115m In, 113m In, 112 In, 111 In), and technetium (99Tc, 99m Tc), thallium (201 Ti), gallium (68Ga, 67Ga), palladium (103 Pd), molybdenum (99Mo), xenon (133 Xe), fluorine (18F), 153 Sm, 177 Lu, 159 Gd, 149 Pm, 140 La, 175 Yb, 166 Ho, 90 Y, 47 Sc, 186 Re, 188 Re, 142 Pr, 105 Rh, 97 Ru; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.

[0387] In addition to assaying levels of polypeptide of the present invention in a biological sample, proteins can also be detected *in vivo* by imaging. Antibody labels or markers for *in vivo* imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable

characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

[0388] A reproductive system antigen-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, 131 I, 112 In, 99m Tc, (131 I, 125 I, 123 I, 121 I), carbon (14C), sulfur (35S), tritium (3H), indium (115mIn, 113mIn, 112In, 111In), and technetium (99Tc, 99mTc), thallium (201Ti), gallium (68Ga, 67Ga), palladium (103Pd), molybdenum (99Mo), xenon (133Xe), fluorine (18F, 153Sm, 177Lu, 159Gd, 149Pm, 140La, 175Yb, 166Ho, 90Y, 47Sc, 186Re, <sup>188</sup>Re, <sup>142</sup>Pr, <sup>105</sup>Rh, <sup>97</sup>Ru), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously or intraperitoneally) into the mammal to be examined for reproductive system disorder. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which express the polypeptide encoded by a polynucleotide of the invention. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments" (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982)).

[0389] In one embodiment, the invention provides a method for the specific delivery of compositions of the invention to cells by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or antibodies) that are associated with heterologous polypeptides or nucleic acids. In one example, the invention provides a method for delivering a therapeutic protein into the targeted cell. In another example, the invention provides a method for delivering a single stranded nucleic acid (e.g., antisense or ribozymes) or double stranded nucleic acid (e.g., DNA that can integrate into the cell's genome or replicate episomally and that can be transcribed) into the targeted cell.

[0390] In another embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.

- [0391] In a preferred embodiment, the invention provides a method for the specific destruction of reproductive system cells (e.g., aberrant reproductive system cells, neoplasms of the reproductive system) by administering polypeptides of the invention (e.g., polypeptides encoded by polynucleotides of the invention and/or antibodies) in association with toxins or cytotoxic prodrugs. In another preferred embodiment the invention provides a method for the specific destruction of tissues/cells corresponding to the library source relating to a polynucleotide sequence of the invention as disclosed in column 7 of Table 1A by administering polypeptides of the invention in association with toxins or cytotoxic prodrugs.
- By "toxin" is meant one or more compounds that bind and activate [0392] endogenous cytotoxic effector systems, radioisotopes, holotoxins, modified toxins, catalytic subunits of toxins, or any molecules or enzymes not normally present in or on the surface of a cell that under defined conditions cause the cell's death. Toxins that may be used according to the methods of the invention include, but are not limited to, radioisotopes known in the art, compounds such as, for example, antibodies (or complement fixing containing portions thereof) that bind an inherent or induced endogenous cytotoxic effector system, thymidine kinase, endonuclease, RNAse, alpha toxin, ricin, abrin, Pseudomonas exotoxin A, diphtheria toxin, saporin, momordin, gelonin, pokeweed antiviral protein, alpha-sarcin and cholera toxin. "Toxin" also includes a cytostatic or cytocidal agent, a therapeutic agent or a radioactive metal ion, e.g., alpha-emitters such as, for example, <sup>213</sup>Bi, or other radioisotopes such as, for example, 103Pd, 133Xe, 131I, 111In, 68Ge, 57Co, 65Zn, 85Sr, 32P, 35S, 90Y, 153Sm, 153Gd, <sup>169</sup>Yb, <sup>51</sup>Cr, <sup>54</sup>Mn, <sup>75</sup>Se, <sup>113</sup>Sn, <sup>90</sup>Yttrium, <sup>117</sup>Tin, <sup>186</sup>Rhenium, <sup>166</sup>Holmium, and 188Rhenium; luminescent labels, such as luminol; and fluorescent labels, such as fluorescein and rhodamine, and biotin.
- [0393] In a specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope <sup>90</sup>Y. In another specific embodiment, the invention provides a method for the specific

destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope <sup>111</sup>In. In a further specific embodiment, the invention provides a method for the specific destruction of cells (e.g., the destruction of tumor cells) by administering polypeptides of the invention or antibodies of the invention in association with the radioisotope <sup>131</sup>I.

[0394] Techniques known in the art may be applied to label polypeptides of the invention (including antibodies). Such techniques include, but are not limited to, the use of bifunctional conjugating agents (see e.g., U.S. Patent Nos. 5,756,065; 5,714,631; 5,696,239; 5,652,361; 5,505,931; 5,489,425; 5,435,990; 5,428,139; 5,342,604; 5,274,119; 4,994,560; and 5,808,003; the contents of each of which are hereby incorporated by reference in its entirety).

[0395] Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression level of a polypeptide of the present invention in cells or body fluid of an individual; and (b) comparing the assayed polypeptide expression level with a standard polypeptide expression level, whereby an increase or decrease in the assayed polypeptide expression level compared to the standard expression level is indicative of a disorder. With respect to cancer, the presence of a relatively high amount of transcript in biopsied tissue from an individual may indicate a predisposition for the development of the disease, or may provide a means for detecting the disease prior to the appearance of actual clinical symptoms. A more definitive diagnosis of this type may allow health professionals to employ preventative measures or aggressive treatment earlier thereby preventing the development or further progression of the cancer.

[0396] Moreover, polypeptides of the present invention can be used to treat or prevent diseases or conditions of the reproductive system such as, for example, reproductive system injury and trauma, infections, neoplastic disorders, congenital defects, and diseases or disorders which result in infertility, complications with pregnancy, labor, or parturition, postpartum difficulties, and as listed below in the section entitled "Reproductive System Disorders". In preferred embodiments, polynucleotides expressed in a particular tissue type (see, e.g., Table 1A, column 7) are used to diagnose, detect, prevent, treat and/or prognose disorders associated with

the tissue type. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B, SOD, catalase, DNA repair proteins), to inhibit the activity of a polypeptide (e.g., an oncogene or tumor supressor), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth inhibition, enhancement of the immune response to proliferative cells or tissues).

[0397] Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease (as described *supra*, and elsewhere herein). For example, administration of an antibody directed to a polypeptide of the present invention can bind, and/or neutralize the polypeptide, and/or reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

[0398] At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the biological activities described herein.

#### **Diagnostic Asssays**

[0399] The compounds of the present invention are useful for diagnosis, treatment, prevention and/or prognosis of various reproductive system related disorders in mammals, preferably humans. Such disorders include, but are not limited to, reproductive system injury and trauma, infections, neoplastic disorders, congenital defects, and diseases or disorders which result in infertility, complications with pregnancy, labor, or parturition, postpartum difficulties, and as listed below in the section entitled "Reproductive System Disorders". In preferred embodiments,

polynucleotides expressed in a particular tissue type (see, e.g., Table 1A, column 7) are used to diagnose, detect, prevent, treat and/or prognose disorders associated with the tissue type.

[0400] Reproductive system antigens are expressed in reproductive system. For a number of reproductive system-related disorders, substantially altered (increased or decreased) levels of reproductive system antigen gene expression can be detected in reproductive system tissue or other cells or bodily fluids (e.g., sera, plasma, urine, semen, synovial fluid or spinal fluid) taken from an individual having such a disorder, relative to a "standard" reproductive system antigen gene expression level, that is, the reproductive system antigen expression level in reproductive system tissues or bodily fluids from an individual not having the reproductive system disorder. Thus, the invention provides a diagnostic method useful during diagnosis of a reproductive system disorder, which involves measuring the expression level of the gene encoding the reproductive system associated polypeptide in reproductive system tissue or other cells or body fluid from an individual and comparing the measured gene expression level with a standard reproductive system antigens gene expression level, whereby an increase or decrease in the gene expression level(s) compared to the standard is indicative of an reproductive system disorder.

[0401] In specific embodiments, the invention provides a diagnostic method useful during diagnosis of a disorder of a normal or diseased tissue/cell source corresponding to column 7 of Table 1A, which involves measuring the expression level of the coding sequence of a polynucleotide sequence associated with this tissue/cell source as disclosed in Table 1A in the tissue/cell source or other cells or body fluid from an individual and comparing the expression level of the coding sequence with a standard expression level of the coding sequence of a polynucleotide sequence, whereby an increase or decrease in the gene expression level(s) compared to the standard is indicative of a disorder of a normal or diseased tissue/cell source corresponding to column 7 of Table 1A.

[0402] In particular, it is believed that certain tissues in mammals with cancer of cells or tissue of the reproductive system express significantly enhanced or reduced levels of normal or altered reproductive system antigen expression and mRNA encoding the reproductive system associated polypeptide when compared to a

corresponding "standard" level. Further, it is believed that enhanced or depressed levels of the reproductive system associated polypeptide can be detected in certain body fluids (e.g., sera, plasma, urine, and spinal fluid) or cells or tissue from mammals with such a cancer when compared to sera from mammals of the same species not having the cancer.

[0403] For example, as disclosed herein, reproductive system associated polypeptides of the invention are expressed in tissues of the reproductive system. Accordingly, polynucleotides of the invention (e.g., polynucleotide sequences complementary to all or a portion of a reproductive system antigen mRNA nucleotide sequence of SEQ ID NO:X, nucleotide sequence encoding SEQ ID NO:Y, nucleotide sequence encoding a polypeptide encoded by SEQ ID NO:X and/or a nucleotide sequence delineated by columns 8 and 9 of Table 2) and antibodies (and antibody fragments) directed against the polypeptides of the invention may be used to quantitate or qualitate concentrations of cells of the reproductive system expressing reproductive system antigens, preferrably on their cell surfaces. These polynucleotides and antibodies additionally have diagnostic applications in detecting abnormalities in the level of reproductive system antigens gene expression, or abnormalities in the structure and/or temporal, tissue, cellular, or subcellular location of reproductive system antigens. These diagnostic assays may be performed in vivo or in vitro, such as, for example, on blood samples, biopsy tissue or autopsy tissue. In specific embodiments, polynucleotides and antibodies of the invention are used to quantitate or qualitate tissues/cells corresponding to the library source disclosed in column 7 of Table 1A expressing the corresponding reproductive system sequence disclosed in the same row of Table 1A, preferrably on their cell surface.

[0404] Thus, the invention provides a diagnostic method useful during diagnosis of a reproductive system disorder, including cancers, which involves measuring the expression level of the gene encoding the reproductive system antigen polypeptide in tissues of the reproductive system or other cells or body fluid from an individual and comparing the measured gene expression level with a standard reproductive system antigen gene expression level, whereby an increase or decrease in the gene expression level compared to the standard is indicative of a reproductive system disorder. In specific embodiments, polynucleotides and antibodies of the invention are used to

quantitate or qualitate tissues/cells corresponding to the library source disclosed in column 7 of Table 1A expressing the corresponding reproductive system sequence disclosed in the same row of Table 1A, preferrably on their cell surface.

[0405] Where a diagnosis of a disorder in the reproductive system, including diagnosis of a tumor, has already been made according to conventional methods, the present invention is useful as a prognostic indicator, whereby patients exhibiting enhanced or depressed reproductive system antigen gene expression will experience a worse clinical outcome relative to patients expressing the gene at a level nearer the standard level.

By "assaying the expression level of the gene encoding the reproductive [0406] system associated polypeptide" is intended qualitatively or quantitatively measuring or estimating the level of the reproductive system antigen polypeptide or the level of the mRNA encoding the reproductive system antigen polypeptide in a first biological sample either directly (e.g., by determining or estimating absolute protein level or mRNA level) or relatively (e.g., by comparing to the reproductive system associated polypeptide level or mRNA level in a second biological sample). Preferably, the reproductive system antigen polypeptide expression level or mRNA level in the first biological sample is measured or estimated and compared to a standard reproductive system antigen polypeptide level or mRNA level, the standard being taken from a second biological sample obtained from an individual not having the disorder or being determined by averaging levels from a population of individuals not having a disorder of the reproductive system. As will be appreciated in the art, once a standard reproductive system antigen polypeptide level or mRNA level is known, it can be used repeatedly as a standard for comparison.

By "biological sample" is intended any biological sample obtained from an individual, cell line, tissue culture, or other source containing reproductive system antigen polypeptides (including portions thereof) or mRNA. As indicated, biological samples include body fluids (such as sera, plasma, urine, synovial fluid and spinal fluid) which contain cells expressing reproductive system antigen polypeptides, tissues of the reproductive system, and other tissue sources found to express the full length or fragments thereof of a reproductive system antigen. Methods for obtaining tissue biopsies and body fluids from mammals are well known in the art. Where the

biological sample is to include mRNA, a tissue biopsy is the preferred source.

Total cellular RNA can be isolated from a biological sample using any suitable technique such as the single-step guanidinium-thiocyanate-phenol-chloroform method described in Chomczynski and Sacchi, Anal. Biochem. 162:156-159 (1987). Levels of mRNA encoding the reproductive system antigen polypeptides are then assayed using any appropriate method. These include Northern blot analysis, S1 nuclease mapping, the polymerase chain reaction (PCR), reverse transcription in combination with the polymerase chain reaction (RT-PCR), and reverse transcription in combination with the ligase chain reaction (RT-LCR).

The present invention also relates to diagnostic assays such as quantitative and diagnostic assays for detecting levels of reproductive system antigen polypeptides, in a biological sample (e.g., cells and tissues), including determination of normal and abnormal levels of polypeptides. Thus, for instance, a diagnostic assay in accordance with the invention for detecting over-expression of reproductive system antigens compared to normal control tissue samples may be used to detect the presence of tumors. Assay techniques that can be used to determine levels of a polypeptide, such as a reproductive system antigen polypeptide of the present invention in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radioimmunoassays, competitive-binding assays, Western Blot analysis and ELISA assays. Assaying reproductive system antigen polypeptide levels in a biological sample can occur using any art-known method.

Sample can occur using antibody-based techniques. For example, reproductive system antigen polypeptide expression in tissues can be studied with classical immunohistological methods (Jalkanen et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-3096 (1987)). Other antibody-based methods useful for detecting reproductive system antigen polypeptide gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and technetium (99mTc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

known, or suspected, to express the reproductive system related antigen gene (such as, for example, cells of the reproductive system or cancers of the reproductive system). The protein isolation methods employed herein may, for example, be such as those described in Harlow and Lane (Harlow, E. and Lane, D., 1988, "Antibodies: A Laboratory Manual", Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York), which is incorporated herein by reference in its entirety. The isolated cells can be derived from cell culture or from a patient. The analysis of cells taken from culture may be a necessary step in the assessment of cells that could be used as part of a cell-based gene therapy technique or, alternatively, to test the effect of compounds on the expression of the reproductive system related antigen gene.

- [0412] For example, antibodies, or fragments of antibodies, such as those described herein, may be used to quantitatively or qualitatively detect the presence of reproductive system related antigen gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.
- [0413] In a preferred embodiment, antibodies, or fragments of antibodies directed to any one or all of the predicted epitope domains of the reproductive system related antigen polypeptides (Shown in Table 1A, column 6) may be used to quantitatively or qualitatively detect the presence of reproductive system related antigen gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.
- [0414] In an additional preferred embodiment, antibodies, or fragments of antibodies directed to a conformational epitope of a reproductive system related antigen may be used to quantitatively or qualitatively detect the presence of reproductive system related antigen gene products or conserved variants or peptide fragments thereof. This can be accomplished, for example, by immunofluorescence techniques employing a fluorescently labeled antibody coupled with light microscopic, flow cytometric, or fluorimetric detection.
- [0415] The antibodies (or fragments thereof), and/or reproductive system related

antigen polypeptides of the present invention may, additionally, be employed histologically, as in immunofluorescence, immunoelectron microscopy or non-immunological assays, for in situ detection of reproductive system related antigen gene products or conserved variants or peptide fragments thereof. In situ detection may be accomplished by removing a histological specimen from a patient, and applying thereto a labeled antibody or reproductive system related antigen polypeptide of the present invention. The antibody (or fragment thereof) or reproductive system related antigen polypeptide is preferably applied by overlaying the labeled antibody (or fragment) onto a biological sample. Through the use of such a procedure, it is possible to determine not only the presence of the reproductive system related antigen gene product, or conserved variants or peptide fragments, or reproductive system related antigen polypeptide binding, but also its distribution in the examined tissue. Using the present invention, those of ordinary skill will readily perceive that any of a wide variety of histological methods (such as staining procedures) can be modified in order to achieve such in situ detection.

Immunoassays and non-immunoassays for reproductive system related antigen gene products or conserved variants or peptide fragments thereof will typically comprise incubating a sample, such as a biological fluid, a tissue extract, freshly harvested cells, or lysates of cells which have been incubated in cell culture, in the presence of a detectably labeled antibody capable of binding reproductive system related antigen gene products or conserved variants or peptide fragments thereof, and detecting the bound antibody by any of a number of techniques well-known in the art.

onto a solid phase support or carrier such as nitrocellulose, or other solid support which is capable of immobilizing cells, cell particles or soluble proteins. The support may then be washed with suitable buffers followed by treatment with the detectably labeled anti- reproductive system related antigen antibody or detectable reproductive system related antigen polypeptide. The solid phase support may then be washed with the buffer a second time to remove unbound antibody or polypeptide. Optionally the antibody is subsequently labeled. The amount of bound label on solid support may then be detected by conventional means.

[0418] By "solid phase support or carrier" is intended any support capable of

binding an antigen or an antibody. Well-known supports or carriers include glass, polystyrene, polypropylene, polyethylene, dextran, nylon, amylases, natural and modified celluloses, polyacrylamides, gabbros, and magnetite. The nature of the carrier can be either soluble to some extent or insoluble for the purposes of the present invention. The support material may have virtually any possible structural configuration so long as the coupled molecule is capable of binding to an antigen or antibody. Thus, the support configuration may be spherical, as in a bead, or cylindrical, as in the inside surface of a test tube, or the external surface of a rod. Alternatively, the surface may be flat such as a sheet, test strip, etc. Preferred supports include polystyrene beads. Those skilled in the art will know many other suitable carriers for binding antibody or antigen, or will be able to ascertain the same by use of routine experimentation.

[0419] The binding activity of a given lot of anti- reproductive system related antigen antibody or reproductive system related antigen polypeptide may be determined according to well known methods. Those skilled in the art will be able to determine operative and optimal assay conditions for each determination by employing routine experimentation.

levels or polynucleotide levels in a biological sample obtained from an individual, reproductive system related antigen polypeptide or polynucleotide can also be detected in vivo by imaging. For example, in one embodiment of the invention, reproductive system related antigen polypeptide and/or anti- reproductive system related antigen antibodies are used to image reproductive system diseased cells, such as neoplasms. In another embodiment, reproductive system related antigen polynucleotides of the invention (e.g., polynucleotides complementary to all or a portion of reproductive system related antigen mRNA) and/or anti- reproductive system related antigen antibodies (e.g., antibodies directed to any one or a combination of the epitopes of reproductive system related antigens, antibodies directed to the full length polypeptide expressed on the cell surface of a mammalian cell) are used to image diseased or neoplastic cells of the reproductive system.

[0421] Antibody labels or markers for in vivo imaging of reproductive system